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This paper is dedicated to Dr. Raymond N. Castle on the occasion of his obituary notice for his brilliant achievements and his numerous editorial contributions in the field of heterocyclic chemistry.

The equimolar mixture of *N*-(hydroxyalkyl)pyrazoles and borane formed boric ester complex, in which the remaining borane was stabilized by the adjacent nitrogen of the pyrazole ring. The borane complex derived from the chiral pyrazoles such as 3-phenyl-*l*-menthopyrazole reduced *p*-methylacetophenone (**21**) enantioselectively. When (2'*S*)-2-(2'-phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole ((2'*S*)-**10b**) was used, **21** was reduced into (*S*)-*p*-methylphenyl-1-ethanol (**22**) in moderate chemical and optical yields. Due to the inconvenience of the preparation and the lower optical yield, the use of *N*-(α -hydroxyalkyl)pyrazoles was unpromising for the enantioselective reduction of ketones by borane.

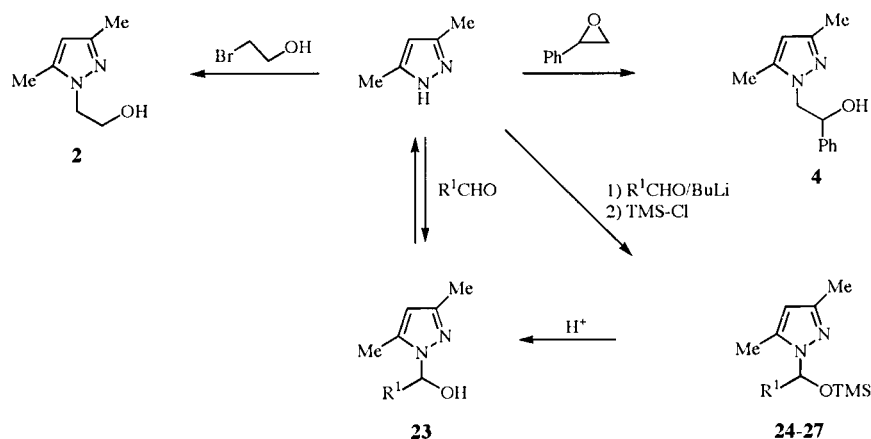
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Recently we have developed the preparation and tested the utilities of 3-phenyl-*l*-menthopyrazole (**1**) as a new chiral auxiliary [1], which has unique structure and properties different from the conventional chiral auxiliaries [2]. The most important characteristics of this auxiliary are that the substrate terminates to the nitrogen atom of the heteroaromatic pyrazole ring, and that the substrate is surrounded by the chiral atmosphere. This structural feature causes the diastereofacial attack on the substrate moiety in the reactions with alkyl halides [3], diphenyldisulfide [4], acyl chloride [5], aldehydes [6], and C=N compounds [7]. Moreover, the asymmetric additions of Grignard reagents [8], dienes [9] and 1,3-dipolar compounds [10] on 2-(α,β -unsaturated)acyl-3-phenyl-*l*-menthopyrazoles have been reported. Otherwise, *N*-acylheteroaromatics such as *N*-acylimidazoles are utilized as the activated acyl moiety in a wide varieties of organic syntheses [11]. As an analogue of these *N*-acylheteroaromatics, *N*-acylpyrazoles are

easily converted into acyl derivatives by the action of nucleophiles such as alcohols [12], amines [13], Grignard reagents [14], or organozinc compounds [15] under basic or acidic conditions. As a part of these investigations, we have been strongly desired to develop the catalytic use of pyrazole derivatives in the synthetic reactions especially in the asymmetric reactions.

In the literature, there are some papers of chiral amino alcohols, which are utilized as asymmetric catalysts for the borane reduction of ketones. The hydroxyl moiety of these amino alcohols reacts with borane to form boric esters, and the amino moiety takes the role of a Lewis base. Subsequently the rigid structure of borane complex such as oxazaborolidine sterically regulated the reduction of ketones [16]. Since *l*-menthopyrazole derivatives exhibited both the characteristics of Lewis basicity and the asymmetric structure, introduction of the hydroxyl group was expected to exploit the utilities of the *l*-menthopyrazoles as chiral catalysts for the borane

Scheme 1



reduction. Here we will report the preparation and the behaviors of *l*-menthopyrazoles having the hydroxylalkyl group.

Results and Discussion.

N-(2'-Hydroxyalkyl)pyrazole.

N-(2'-Hydroxyalkyl)pyrazoles were directly prepared from pyrazoles with halo alcohols or epoxides. In the high pressure reactor, 3,5-dimethylpyrazole was heated with 2-bromoethanol to give 1-(2'-hydroxyethyl)-3,5-dimethylpyrazole (**2**) in good yield. Also **2** was prepared by the reduction of 1-carbomethoxymethyl-3,5-dimethylpyrazole (**3**) in good yield. By the treatment of 3,5-dimethylpyrazole with styrene oxide, 1-(2'-hydroxy-2'-phenylethyl)-3,5-dimethylpyrazole (**4**) was obtained.

Since hydrogen was evolved by mixing **4** with borane, the volume of evolved hydrogen was measured by gas burette. An equimolar amount of hydrogen was evolved on a few minutes and then it ceased completely, and another 2 molar amount of hydrogen evolution was observed by the

quenching with hydrochloric acid, plotted in Figure 1. On the other hand, tetrahydrofuran (THF) solution of borane evolved an equimolar amount of hydrogen gradually over one hour. These facts suggested that **4** reacted with borane to form boric ester, and that borane was stabilized by the adjacent nitrogen atom of the pyrazole ring.

By the treatment with borane, the ^1H NMR peaks of **4** were all shifted down field particularly those of peaks corresponding to hydrogens on the pyrazole ring. These down field shifts gave a hint of N-B bond formation. Therefore an ^{11}B NMR spectral study was undertaken to elucidate the situation of boron atom. The singlet peak of triethoxyborane (**7**) appeared at -0.22 ppm, while THF solution of borane showed a quartet at -18.69 ppm ($J = 106.8$ Hz). By the addition of 1,3,5-trimethylpyrazole, the quartet peak of borane was shifted to -40.59 ppm ($J = 97.04$ Hz) by the N-B chelation. The equimolar mixture of borane and ethanol gave the peaks of diethoxyborane (**6**) at 9.08 ppm (doublet, $J = 159.9$ Hz), and the peaks of borane and **7**, but the triplet signal of ethoxyborane (**5**) could not be detected. In the equimolar mixture of borane and **7**, the doublet peak of **6** was observed as well as the peaks of borane and **7**. The quartet of borane chelated to the pyrazole nitrogen and boric ester the singlet appeared in the ^{11}B NMR spectrum of the equimolar mixture of borane and **4**, and any doublet or triplet peak could not be detected. From Table 1 of these spectral observations, we concluded that of borane was converted into boric ester by the action of alcohol, which was equilibrated into trialkoxyborane. The residual borane was stabilized by the chelation with pyrazole nitrogen.

The evolution of hydrogen and the ^{11}B NMR study lead us to the possibility of asymmetric induction on the borane reduction of prochiral ketones catalyzed by the optically active pyrazole. Thus *N*-(2'-hydroxyalkyl)-3-phenyl-*l*-menthopyrazoles were postulated as chiral pyrazoles for catalyst. When **1** was treated with 2-bromoethanol, the regio-

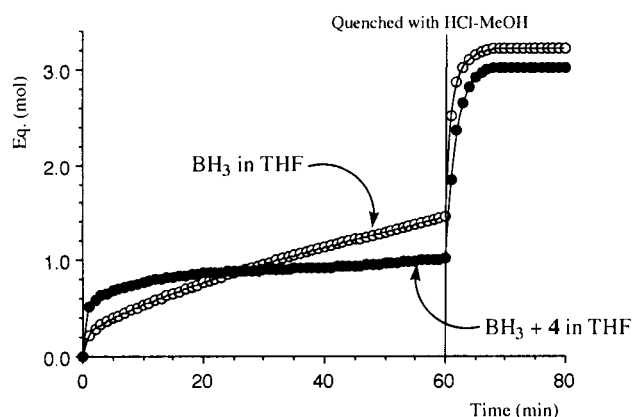


Figure 1. H_2 Evolution from BH_3 with **4**.

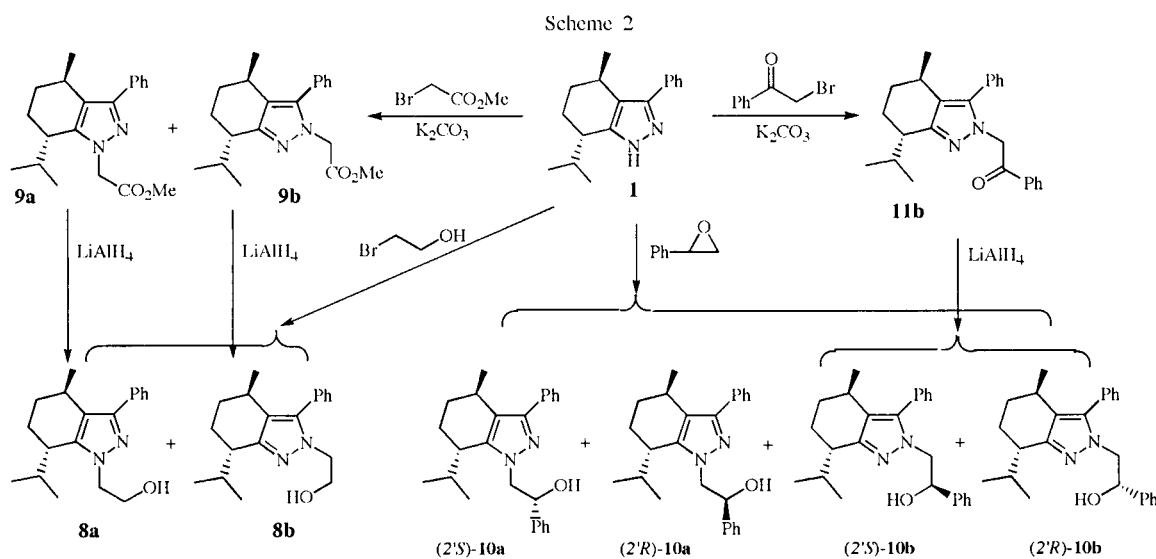


Table 1
 ^{11}B NMR of BH_3 -Pyrazole Complex in THF

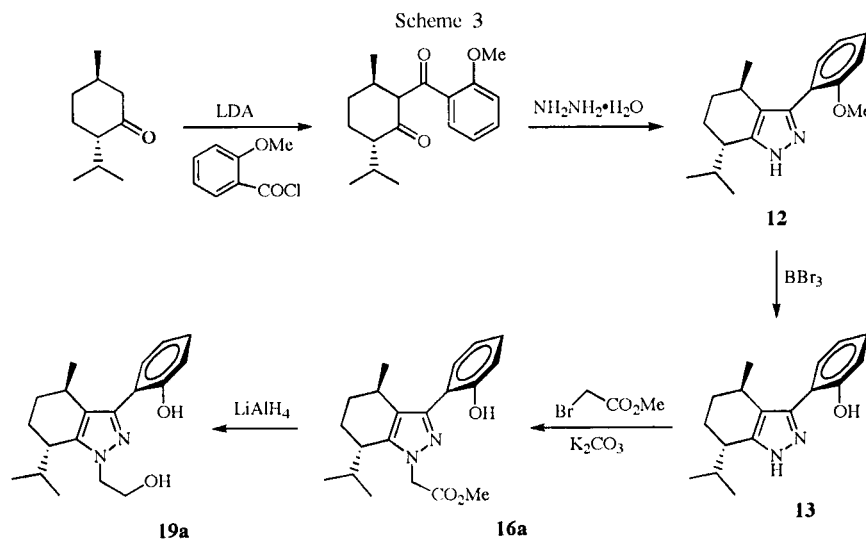
Entry	Borane	Additive	δ [a]	Assignment
1	BH_3		-18.69 (q, $J = 106.8$ Hz)	BH_3
2	$\text{B}(\text{OEt})_3$ (7)		-0.22 (s)	$\text{B}(\text{OR})_3$
3	BH_3	EtOH	-18.69 (q, $J = 106.8$ Hz) 9.08 (d, $J = 159.9$ Hz) -0.22 (s)	BH_3 $\text{BH}(\text{OR})_2$ $\text{B}(\text{OR})_3$
4	BH_3	$\text{B}(\text{OEt})_3$ (7)	-18.69 (q, $J = 106.8$ Hz) 9.08 (d, $J = 159.9$ Hz) -0.22 (s)	BH_3 $\text{BH}(\text{OR})_2$ $\text{B}(\text{OR})_3$
5	BH_3	1,3,5-Trimethylpyrazole	-40.59 (q, $J = 97.04$ Hz)	$\text{BH}_3 \cdots \text{Pyrazole}$
6	BH_3	2	-40.47 (q, $J = 97.04$ Hz) 1.81 (s)	$\text{BH}_3 \cdots \text{Pyrazole}$ $\text{B}(\text{OR})_3$
7	BH_3	4	-40.23 (q, $J = 90.94$ Hz) 1.88 (s)	$\text{BH}_3 \cdots \text{Pyrazole}$ $\text{B}(\text{OR})_3$

[a] $\text{B}(\text{OMe})_3$ was used as the external standard.

isomeric mixture of 1- (**8a**) and 2-(2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazoles (**8b**) was obtained. Similarly **1** was treated with methyl bromoacetate to afford the regio isomeric mixture of 1- (**9a**) and 2-carbomethoxymethyl-3-phenyl-*l*-menthopyrazole (**9b**), which were separated easier than that of *N*-(2'-hydroxyethyl)pyrazoles (**8**). The isomerically pure **9a** and **9b** were independently reduced by lithium aluminum hydride to give **8a** and **8b**, respectively. In the high pressure reactor, the regio- and diastereoisomers of *N*-(2'-phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole (**10**) were obtained from styrene oxide with **1**. The isomer ratio of these 4 isomers, (2'*S*)-**10a**:(2'*R*)-**10a**:(2'*S*)-**10b**:(2'*R*)-**10b** was found to be 1.3:0.3:1.0:1.0. The isomeric separation was successful by means of silica gel column chromatography. When (*S*)-styrene oxide was treated with

1, two isomers (2'*S*)-**10a** and (2'*S*)-**10b** were formed. Otherwise, 2-benzoylmethyl-3-phenyl-*l*-menthopyrazole (**11b**) was exclusively obtained by the reaction of **1** with α -bromoacetophenone. This carbonyl compound (**11b**) was reduced to the mixture of (2'*S*)-**10b** and (2'*R*)-**10b** by lithium aluminum hydride. The conformational structures of these isomers were deduced by the comparison of their spectral and chromatographic properties.

3-(2'-Methoxy)phenyl-*l*-menthopyrazole (**12**) was converted into 3-(2'-hydroxy)phenyl-*l*-menthopyrazole (**13**) in good yield by the treatment with BBr_3 . Moreover, the various *N*-hydroxyethylpyrazoles (**18-20**) were prepared from 3-(2'-methoxy)phenyl- (**12**), 3-(2'-hydroxy)phenyl- (**13**) and 3-(1'-naphthyl)-*l*-menthopyrazole (**14**) through the corresponding *N*-carbomethoxymethyl pyrazoles (**15-17**).



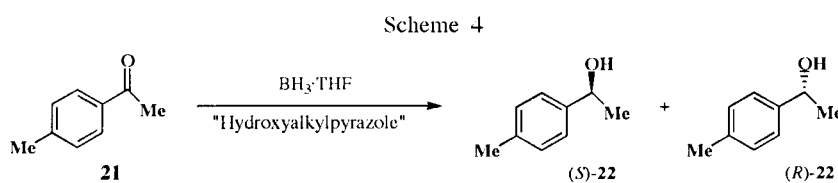


Table 2
Enantioselective BH_3 Reduction of *p*-Methylacetophenone (**21**) Catalyzed by *N*-(2'-Hydroxyethyl)-3-aryl-*l*-menthopyrazoles

Entry	<i>N</i> -(2'-Hydroxyethyl)-3-aryl- <i>l</i> -menthopyrazole		Solvent	Yield % [a]	Ee (Conf.) % [b]	Recover of Cat. %
	R	Ar				
1 8b	H	Ph	THF	35	14 (<i>S</i>)	90
2 8b	H	Ph	Toluene	73	19 (<i>S</i>)	91
3 8b	H	Ph	Hexane	73	30 (<i>S</i>)	89
4 (2' <i>S</i>)- 10b	(<i>S</i>)-Ph	Ph	THF	56	33 (<i>S</i>)	65
5 (2' <i>S</i>)- 10b	(<i>S</i>)-Ph	Ph	Hexane	51	46 (<i>S</i>)	67
6 (2' <i>R</i>)- 10b	(<i>R</i>)-Ph	Ph	THF	34	15 (<i>R</i>)	60
7 (2' <i>R</i>)- 10b	(<i>R</i>)-Ph	Ph	Hexane	82	18 (<i>R</i>)	93
8 8a	H	Ph	THF	51	8 (<i>R</i>)	86
9 8a	H	Ph	Hexane	68	10 (<i>R</i>)	88
10 (2' <i>S</i>)- 10a	(<i>S</i>)-Ph	Ph	THF	69	41 (<i>R</i>)	89
11 (2' <i>S</i>)- 10a	(<i>S</i>)-Ph	Ph	Hexane	57	33 (<i>R</i>)	71
12 18b	H	2'-MeO-C ₆ H ₄	Hexane	75	27 (<i>S</i>)	92
13 19b	H	1'-Naphth	Hexane	50	23 (<i>S</i>)	92
14 20a	H	2'-HO-C ₆ H ₄	Hexane	1	5 (<i>S</i>)	86

[a] Isolated yield. [b] Enantiomer excess was determined by chiral gas chromatography.

These *N*-(2'-hydroxyalkyl)-3-aryl-*l*-menthopyrazoles (**8**, **10** and **18-20**) were resembled to the chiral amino alcohols, which were extensively used as the catalyst for the asymmetric borane reduction of prochiral ketones. Therefore the reduction of *p*-methylacetophenone (**21**) was undertaken by borane to afford *p*-methylphenyl-1-ethanol (**22**) in the presence of *N*-(2'-hydroxyalkyl)pyrazoles. Firstly the reaction conditions were optimized by the reduction of **21** with borane in the presence of **2**. No reduction of **21** was observed with borane in the presence of **2** at room temperature, while **22** was yielded in 49% in the absence of **2**. This fact suggested that the borane complex was exclusively formed with **2**, and free borane did not remain. By the use of an equimolar amount of **2** with borane in THF at 80 °C, **21** was reduced in 23% yield. Since the borane complex with nitrogen on pyrazole was rather stable in hexane, the yield of **22** was improved in hexane solution at 80 °C.

When **21** was reduced by borane in the presence of **8a** under the optimal conditions, optically active **22** with 10% ee (*R*) was obtained in good yield with the high recovery of **8a**. The regioisomer **8b** acted more efficiently as the chiral catalyst for this reaction, and gave (*S*)-**22** in 30% ee. In the presence of (2'*S*)-**10a**, (2'*S*)-**10b** and (2'*R*)-**10b**, **21** was reduced by borane to afford optically active **22**, listed in Table 2. As the results, the most effective catalyst was (2'*S*)-**10b** for this asymmetric reduction, and the (2'*R*)-phenyl group of (2'*R*)-

10b offset the asymmetric effect of menthopyrazole ring. Similarly the substituent effect on the 3-aryl group of *l*-menthopyrazoles was examined by the use of **18-20**. The more bulky 3-substituent on menthopyrazole prevented the action of the chiral catalyst. Although **19a** was expected to form the rigid complex on two hydroxyl groups and pyrazole nitrogen, the reduction of **21** was strongly depressed and (*S*)-**22** was obtained only in 1% yield with 5% ee.

N-(1'-Hydroxyalkyl)pyrazoles.

When 3,5-dimethylpyrazole was treated with propanal in an NMR tube, new peaks of 1-(1'-hydroxypropyl)-3,5-dimethylpyrazole (**23**) appeared along with the peaks attributable to 3,5-dimethylpyrazole and propanal. The relative peak intensity of **23** was proportional to the ratio of aldehyde to pyrazole. The structure of **23** was deduced by the comparison of NMR spectrum with that of 1-(1'-trimethylsilyloxypropyl)-3,5-dimethylpyrazole (**24**). Similar reaction was observed in the cases of isobutyraldehyde and benzaldehyde. Phenylpropionaldehyde gave the mixture of *syn* and *anti* isomers, which were separately isolated as the silylated derivatives. These silyl ethers were hydrolyzed into the corresponding aldehydes and 3,5-dimethylpyrazole. These facts suggested that the mixture of aldehyde and pyrazole was equilibrated to **23** and the isolation of **23** was unfortunately impossible.

Otherwise, the reaction of *N*-acylpyrazoles with organometallic compounds such as Grignard reaction [14] and Reformatsky reaction [15] afforded the ketones and the further reaction to form the corresponding alcohols could not be observed. Similarly *N*-acylpyrazoles was reduced into aldehydes by lithium aluminum hydride [17]. In these reactions, the carbonyl group was speculated to be formed in the term of work up, and the reaction intermediate was likely the metal complex of *N*-(1'-hydroxylalkyl)pyrazole, which resembled the structure of oxazaborolidine. Therefore the borane reduction of ketones was performed in the presence of such metal complex of *N*-(1'-hydroxylalkyl)pyrazole.

Under an argon atmosphere, 2-benzoyl-3-phenyl-*l*-menthopyrazole (**28**) was reduced by equimolar amount of lithium aluminum hydride to form the aluminum complex. Borane THF solution was added to this aluminum complex, and then **21** was treated for 17 hours at -5 °C. Consequently (*S*)-**22** was obtained in 80% yield with 1% ee. When the borane reduction of **21** was performed in the presence of the reaction mixture of **28** with ethylmagnesium iodide, (*S*)-**22** was formed in 19% yield with 11% ee. In both cases, 3-phenyl-*l*-menthopyrazole (**1**) was recovered in high yields. These results suggested that the use of *N*-(1'-hydroxylalkyl)pyrazoles was unpromising for the enantioselective reduction of ketones by borane.

Conclusion.

The equimolar mixture of *N*-(2'-hydroxylalkyl)pyrazoles and borane formed boric ester complex, in which remaining borane was stabilized by the adjacent nitrogen of pyrazole ring. The borane complex derived from the chiral pyrazoles such as 3-phenyl-*l*-menthopyrazole reduced *p*-methylacetophenone (**21**) enantioselectively. When (2'*S*)-2-(2'-phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole ((2'*S*)-**10b**) was used, **21** was reduced into (*S*)-*p*-methylphenyl-1-ethanol (**22**) in moderate chemical and optical yields. Due to the inconvenience of the preparation and the lower optical yield, the use of *N*-(1'-hydroxylalkyl)pyrazoles was unpromising for the enantioselective reduction of ketones by borane.

EXPERIMENTAL

Melting points are uncorrected. ¹H NMR and ¹³C NMR spectra were obtained on JEOL JNM-EX270 (270 MHz) or Varian GEMINI 2000 (200 MHz) spectrometers in deuteriochloroform with tetramethylsilane as an internal standard. The IR spectra were measured by Shimadzu IR-460 spectrophotometer. Specific rotations were measured on JASCO DIP-370 digital polarimeter. The enantiomer ratios were evaluated from the peak ratios of gas chromatography on SHIMADZU GC-14A gas chromatograph using Chrompack Chirasil DEX-CB capillary column (0.25 mm x 25 m). The yields of the products were evaluated by GL Science GC-353 gas chromatograph using dimethylsiloxane type capillary column (0.25 mm x 30 m) of GL Science TC-1. The reactions under high pressure conditions over 700 Mpa were carried out in the Hikari Koatsu Kiki 15-B type High Pressure Reactor.

Preparation of 3-Aryl-*l*-menthopyrazoles.

According to the preparative method of 3-phenyl-*l*-menthopyrazole [3], *l*-menthone (4.0 mmol) was treated with aroyl chloride (4.7 mmol) in the presence of lithium diisopropylamide in dry THF. The mixture of subsequent aroyl-*l*-menthone and hydrazine hydrate in methanol was refluxed in the presence of hydrazine hydrochloride for 17 hours. The product was extracted with ether, washed with dilute hydrochloric acid, water, saturated sodium hydrogen carbonate and saturated sodium chloride, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was purified by silica gel column chromatography with hexane-benzene mixture.

3-(2'-Methoxyphenyl)-*l*-menthopyrazole (**12**).

This compound is obtained in yield 100%; ¹H NMR; δ 0.85 (3H, d, *J* = 7 Hz), 0.91 (3H, d, *J* = 7 Hz), 1.04 (3H, d, *J* = 7 Hz), 1.13-1.34 (1H, m), 1.47-1.61 (1H, m), 1.80-1.90 (1H, m), 1.97-2.07 (1H, m), 2.32-2.39 (1H, m), 2.63-2.71 (1H, m), 2.94-3.02 (1H, m), 3.82 (3H, s), 6.86-7.00 (2H, m), 7.28-7.45 (2H, m), 10.20 (1H, broad s).

Anal. Calcd. for C₁₈H₂₄N₂O: C, 76.02; H, 8.51; N, 9.85. Found: C, 74.90; H, 8.46; N, 9.71.

3-(1'-Naphthyl)-*l*-menthopyrazole (**14**).

This compound is obtained in yield 55%; ¹H NMR; δ 0.51 (3H, d, *J* = 7 Hz), 0.72 (3H, d, *J* = 7 Hz), 0.90 (3H, d, *J* = 7 Hz), 0.99-1.21 (1H, m), 1.46-1.58 (1H, m), 1.80-1.96 (2H, m), 2.23-2.30 (1H, m), 2.58-2.76 (2H, m), 2.30-2.48 (4H, m), 2.74-2.84 (3H, m), 9.97 (1H, broad s).

Anal. Calcd. for C₂₁H₂₄N₂: C, 82.85; H, 7.95; N, 9.2. Found: C, 81.12; H, 7.88; N, 8.93.

3-(2'-Hydroxyphenyl)-*l*-menthopyrazole (**13**).

To the dichloromethane solution (5 ml) of 3-(2'-methoxyphenyl)-*l*-menthopyrazole (1.65 g, 5.8 mmol), boron tribromide (1.76 g, 7 mmol) in dichloromethane (7 ml) was added at -90 °C, and then the mixture was warmed to room temperature. After stirring for 20 hours, the reaction mixture was quenched with saturated sodium hydrogen carbonate, and extracted with toluene. The organic layer was washed with saturated sodium chloride, dried over anhydrous magnesium sulfate, and concentrated. The residue was purified by silica gel column chromatography with hexane-ethyl acetate mixture; yield 77%; ¹H NMR; δ 0.87 (3H, d, *J* = 6.8 Hz), 1.00 (3H, d, *J* = 6.8 Hz), 1.14 (3H, d, *J* = 6.8 Hz), 1.21-1.33 (2H, m), 1.60-2.14 (4H, m), 2.53-2.61 (1H, m), 3.19-3.28 (1H, m), 6.87-7.05 (2H, m), 7.15-7.25 (1H, m), 7.60-7.65 (1H, m).

Anal. Calcd. for C₁₇H₂₂N₂O: C, 75.52; H, 8.2; N, 10.36. Found: C, 75.39; H, 8.20; N, 10.42.

The Preparation of *N*-(2'-Hydroxyethyl)pyrazole by High Pressure Method.

The benzene solution (3.5 ml) of the appropriate pyrazole (2 mmol) and 2-bromoethanol (660 mg, 5.3 mmol) was heated at 80 °C under 800 Mpa for 14 hours in the high pressure reactor. After removal of the solvent, the residue was extracted with ether and the organic layer was washed 3 times with aqueous sodium hydroxide, water, and saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. The residue was purified by silica gel column chromatography with hexane-ethyl acetate mixture.

1-(2'-Hydroxyethyl)-3,5-dimethylpyrazole (2).

This compound is obtained in yield 72%; mp 75-76 °C (from Hexane); ¹H NMR; δ 2.20 (3H, s), 2.23 (3H, s), 3.94-4.05 (4H, AB, *J* = 5.2 Hz), 5.80 (1H, s), 7.27 (1H, s).

Anal. Calcd. for C₇H₁₂N₂O: C, 59.98; H, 8.63; N, 19.98. Found: C, 60.07; H, 8.77; N, 20.02.

1-(2'-Phenyl-2'-hydroxyethyl)-3,5-dimethylpyrazole (4).

This compound is obtained in yield 78%; bp 195-200 °C/5 mmHg; ¹H NMR; δ 2.00 (3H, s), 2.24 (3H, s), 4.08 (2H, d-AB, *J* = 14.0, 6.2, 3.2 Hz), 4.84 (1H, broad s), 5.08 (1H, d-d, *J* = 7.4, 3.0 Hz), 5.78 (1H, s), 7.32 (5H, s); ¹³C NMR; δ (DEPT) 10.2 (CH₃), 12.9 (CH₃), 54.4 (CH₂), 73.0 (CH), 104.5 (CH), 125.5 (CH), 127.5 (CH), 128.1 (CH), 147.8 (C), 156.9 (C).

Anal. Calcd. for C₁₃H₁₆N₂O: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.25; H, 7.45; N, 12.95.

Reduction of *N*-(Carbomethoxymethyl)pyrazole.

The mixture of appropriate pyrazole (4 mmol), methyl bromoacetate (5.4 mmol) and anhydrous potassium carbonate (690 mg, 5 mmol) in toluene (10 ml) was refluxed for 17 hours under an argon atmosphere. The reaction mixture was quenched with water, and the organic layer was washed with aqueous sodium hydroxide and saturated sodium chloride. After removal of the solvent, *N*-(carbomethoxymethyl)pyrazole was purified by silica gel column chromatography with hexane-ethyl acetate mixture. Subsequent *N*-(carbomethoxymethyl)pyrazole (1.5 mmol) was reduced by lithium aluminum hydride (65 mg, 1.7 mmol) in anhydrous ether (5 ml) for 1.5 hours at room temperature. After the mixture was quenched with water, the mixture was worked up as described above.

1-Carbomethoxymethyl-3,5-dimethylpyrazole (3).

This compound is obtained in yield 65%; bp 150-160 °C/4 mmHg; mp 40-41 °C; ¹H NMR; δ 2.20 (3H, s), 2.21 (3H, s), 3.76 (3H, s), 4.77 (2H, s), 5.86 (1H, s).

Anal. Calcd. for C₈H₁₂N₂O₂: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.10; H, 7.00; N, 16.64.

1-Carbomethoxymethyl-3-phenyl-*l*-menthopyrazole (9a).

This compound is obtained in yield 32%; mp 72-73 °C (from Hexane); ¹H NMR; δ 0.89 (3H, d, *J* = 6.8 Hz), 0.97 (3H, d, *J* = 6.8 Hz), 1.02 (3H, d, *J* = 7.0 Hz), 1.22-1.29 (2H, m), 1.38-2.11 (2H, m), 2.54-2.59 (1H, m), 3.17-3.25 (1H, m), 3.75 (3H, s), 4.89 (2H, s), 7.26-7.41 (3H, m), 7.69-7.74 (2H, m).

Anal. Calcd. for C₂₀H₂₆N₂O₂: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.50; H, 8.09; N, 8.51.

2-Carbomethoxymethyl-3-phenyl-*l*-menthopyrazole (9b).

This compound is obtained in yield 94%; ¹H NMR; δ 0.76 (3H, d, *J* = 6.6 Hz), 0.86 (3H, d, *J* = 6.6 Hz), 1.06 (3H, d, *J* = 6.9 Hz), 1.23-1.27 (1H, m), 1.45-1.58 (1H, m), 1.83-1.98 (2H, m), 2.43-2.50 (1H, m), 2.67-2.82 (2H, m), 3.66 (3H, s), 4.70 (2H, AB, *J* = 29.4 Hz), 7.30-7.43 (5H, m).

Anal. Calcd. for C₂₀H₂₆N₂O₂: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.48; H, 7.74; N, 8.57.

2-Carbomethoxymethyl-3-(2'-methoxyphenyl)-*l*-menthopyrazole (15b).

This compound is obtained in yield 55%; ¹H NMR; δ 0.70 (3H, d, *J* = 6.8 Hz), 0.86 (3H, d, *J* = 6.8 Hz), 1.05 (3H, d, *J* = 7

Hz), 1.16-2.00 (4H, m), 2.39-2.89 (3H, m), 3.61 (3H, s), 3.77 (3H, s), 4.53-5.35 (2H, m), 6.88-7.43 (4H, m).

Anal. Calcd. for C₂₁H₂₈N₂O₃: C, 70.76; H, 7.92; N, 7.86. Found: C, 70.71; H, 7.94; N, 7.52.

1-Carbomethoxymethyl-3-(2'-hydroxyphenyl)-*l*-menthopyrazole (16a).

This compound is obtained in yield 77%; ¹H NMR; δ 0.89 (3H, d, *J* = 6.8 Hz), 1.00 (3H, d, *J* = 6.9 Hz), 1.11 (3H, d, *J* = 6.9 Hz), 1.24-1.54 (1H, m), 1.76-2.09 (4H, m), 2.51-2.56 (1H, m), 3.31-3.36 (1H, m), 3.73 (3H, s), 4.84 (2H, d, *J* = 1.7 Hz), 5.36-7.70 (4H, m).

2-Carbomethoxymethyl-3-(1'-naphtyl)-*l*-menthopyrazole (17b).

This compound is obtained in yield 13%. *Major Isomer.* ¹H NMR; δ 0.52 (3H, d, *J* = 6.9 Hz), 0.93 (3H, d, *J* = 6.9 Hz), 1.10 (3H, d, *J* = 6.9 Hz), 1.21-1.33 (1H, m), 1.50-1.63 (1H, m), 1.83-2.60 (2H, m), 2.71-2.85 (1H, m), 3.53 (3H, s), 4.65 (2H, AB, *J* = 17.5 Hz), 7.434-7.59 (5H, m). *Minor Isomer.* ¹H NMR; δ 0.52 (3H, d, *J* = 6.9 Hz), 0.92 (3H, d, *J* = 6.9 Hz), 1.10 (3H, d, *J* = 6.9 Hz), 1.21-1.33 (1H, m), 1.50-1.63 (1H, m), 1.83-2.60 (2H, m), 2.71-2.85 (1H, m), 3.54 (3H, s), 4.66 (2H, AB, *J* = 17.5 Hz), 7.434-7.59 (5H, m), 7.87-7.92 (2H, m).

2-(2'-Hydroxyethyl)-3-(2'-methoxyphenyl)-*l*-menthopyrazole (18b).

This compound is obtained in yield 83%; ¹H NMR; δ 0.69 (3H, d, *J* = 6.6 Hz), 0.89 (3H, d, *J* = 6.9 Hz), 1.05 (3H, d, *J* = 6.9 Hz), 1.23-1.31 (1H, m), 1.46-1.51 (1H, m), 1.81-1.96 (2H, m), 2.35-2.42 (1H, m), 2.65-2.75 (2H, m), 3.79 (3H, s), 3.82-4.00 (4H, m), 6.94-7.03 (2H, m), 7.15-7.27 (1H, m), 7.35-7.43 (1H, m).

Anal. Calcd. for C₂₀H₂₈N₂O₂: C, 73.14; H, 8.59; N, 8.53. Found: C, 72.62; H, 8.33; N, 8.25.

2-(2'-Hydroxyethyl)-3-(1'-naphtyl)-*l*-menthopyrazole (19b).

This compound is obtained in yield 64%; mp 116-117 °C (from Hexane); ¹H NMR; δ 0.55 (3H, d, *J* = 6.8 Hz), 0.95 (3H, d, *J* = 6.8 Hz), 1.10 (3H, d, *J* = 7.0 Hz), 1.22-1.34 (1H, m), 1.47-1.64 (1H, m), 1.84-1.94 (2H, m), 2.45-2.58 (2H, m), 2.72-2.81 (1H, m), 3.66-4.02 (4H, m), 7.26-7.58 (5H, m), 7.90-7.95 (2H, m).

Anal. Calcd. for C₂₃H₂₈N₂O: C, 79.27; H, 8.1; N, 8.04. Found: C, 79.18; H, 8.32; N, 7.99.

1-(2'-Hydroxyethyl)-3-(2'-methoxyphenyl)-*l*-menthopyrazole (20a).

This compound is obtained in yield 77%; ¹H NMR; δ 0.91 (3H, d, *J* = 6.8 Hz), 1.01 (3H, d, *J* = 7 Hz), 1.10 (3H, d, *J* = 6.6 Hz), 1.43-2.15 (5H, m), 2.65-2.72 (1H, m), 3.30-3.40 (1H, m), 3.97-4.40 (4H, m), 6.86-7.03 (2H, m), 7.14-7.26 (1H, m), 7.66-7.71 (1H, m).

Anal. Calcd. for C₁₉H₂₆N₂O₂: C, 72.58; H, 8.34; N, 8.91. Found: C, 72.27; H, 8.12; N, 8.74.

The Preparation of *N*-(2'-Phenyl-2'-hydroxyethyl)pyrazole by High Pressure Method.

The benzene solution (3.5 ml) of the appropriate pyrazole (2 mmol) and styrene oxide (480 mg, 4 mmol) was heated at 80 °C under 800 Mpa for 14 hours in the high pressure reactor. The reaction mixture work up was like that of *N*-(2'-hydroxyethyl)pyrazole.

(2'S)-1-(2'-Phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole ((2'S)-10a).

This compound is obtained in yield 25%; mp 46-47 °C; ¹H NMR; δ 0.79 (3H, d, *J* = 6.8 Hz), 0.89 (3H, d, *J* = 6.8 Hz), 0.97 (3H, d, *J* = 7.0 Hz), 1.23-2.09 (5H, m), 2.26-2.34 (1H, m), 3.17-3.29 (1H, m), 4.10 (1H, ABX, *J* = 4.4, 13.4 Hz), 4.22 (3H, ABX, *J* = 7.8, 13.8 Hz), 5.14 (1H, ABX, *J* = 4.4, 7.8 Hz), 7.12-7.57 (7H, m), 7.73-7.79 (2H, m).

Anal. Calcd. for C₂₅H₃₀N₂O: C, 80.17; H, 8.07; N, 7.48. Found: C, 79.77; H, 8.21; N, 7.13.

(2'R)-1-(2'-Phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole ((2'R)-10a).

This compound is obtained in yield 5%; ¹H NMR; δ 0.80 (3H, d, *J* = 6.8 Hz), 0.96 (3H, d, *J* = 7 Hz), 0.99 (3H, d, *J* = 7 Hz), 1.21-1.48 (1H, m), 1.51-1.64 (1H, m), 1.75-1.84 (1H, m), 1.85-2.21 (2H, m), 2.53-2.62 (1H, m), 3.04-3.14 (1H, m), 4.10-4.28 (4H, m), 5.55-6.05 (1H, m), 7.24-7.63 (10H, m).

(2'S)-2-(2'-Phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole ((2'S)-10b).

This compound is obtained in yield 39%; ¹H NMR; δ 0.69 (3H, d, *J* = 6.9 Hz), 0.94 (3H, d, *J* = 6.9 Hz), 1.10 (3H, d, *J* = 6.9 Hz), 1.19-2.03 (4H, m), 2.39-2.55 (1H, m), 2.66-2.79 (2H, m), 3.97 (1H, ABX, *J* = 6.9, 13.9 Hz), 4.21 (1H, ABX, *J* = 2.6, 13.9 Hz), 5.06 (1H, d-d, *J* = 2.6, 6.9 Hz), 5.7-5.9 (1H, broad), 6.98-7.02 (2H, m), 7.11-7.14 (2H, m), 7.20-7.28 (3H, m), 7.32-7.41 (3H, m); ¹³C NMR; δ (DEPT) 18.5 (CH₃), 20.8 (CH₃), 20.9 (CH₃), 23.2 (CH₂), 27.5 (CH₂), 30.2 (CH), 33.0 (CH), 41.0 (CH), 54.6 (CH₂), 73.8 (CH), 120.4 (C), 125.9 (CH), 127.5 (CH), 128.3 (CH), 128.5 (CH), 129.9 (CH), 131.3 (C), 140.8 (C), 141.3 (C), 151.7 (C).

Anal. Calcd. for C₂₅H₃₀N₂O: C, 80.17; H, 8.07; N, 7.48. Found: C, 80.05; H, 8.12; N, 7.42.

(2'R)-2-(2'-Phenyl-2'-hydroxyethyl)-3-phenyl-*l*-menthopyrazole ((2'R)-10b).

This compound is obtained in yield 25%; ¹H NMR; δ 0.72 (3H, d, *J* = 6.6 Hz), 0.94 (3H, d, *J* = 6.9 Hz), 1.10 (3H, d, *J* = 6.9 Hz), 1.22-2.03 (5H, m), 2.41-2.50 (1H, m), 2.66-2.85 (2H, m), 3.98 (1H, ABX, *J* = 8.3, 13.9 Hz), 4.09 (1H, ABX, *J* = 3.0, 13.9 Hz), 4.83 (1H, d-d, *J* = 3.0, 8.3 Hz), 5.63-5.70 (1H, broad), 7.10-7.16 (2H, m), 7.17-7.20 (2H, m), 7.23-7.32 (3H, m), 7.33-7.42 (3H, m); ¹³C NMR; δ (DEPT) 18.3 (CH₃), 20.6 (C), 20.8 (CH₃), 23.1 (CH₂), 27.4 (CH₂), 30.0 (CH), 32.7 (CH), 41.0 (CH), 55.3 (CH₂), 73.9 (CH), 120.7 (C), 126.0 (CH), 127.7 (CH), 128.3 (CH), 128.5 (C), 129.7 (C), 131.1 (C), 140.4 (C), 140.9 (C), 151.7 (C).

Anal. Calcd. for C₂₅H₃₀N₂O: C, 80.17; H, 8.07; N, 7.48. Found: C, 79.66; H, 8.05; N, 7.33.

Reduction of *N*-(Benzoylmethyl)pyrazole.

The mixture of appropriate pyrazole (2 mmol), α-bromoacetophenone (2.1 mmol) and anhydrous potassium carbonate (350 mg, 2.5 mmol) in toluene (6 ml) was refluxed for 23 hours under argon atmosphere. The reaction mixture was quenched with water, and the organic layer was washed with aqueous sodium hydroxide and saturated sodium chloride. After removal of the solvent, *N*-(benzoylmethyl)pyrazole was purified by silica gel column chromatography with hexane-ethyl acetate mixture. Subsequent *N*-(benzoylmethyl)pyrazole (0.5 mmol) was reduced by lithium aluminum hydride (60 mg, 1.6 mmol) in anhydrous ether (4 ml) for 1.5 hours at room temperature. After the mixture was quenched with water, the mixture was worked up as described above.

2-(Benzoylmethyl)-3-phenyl-*l*-menthopyrazole (11b).

This compound is obtained in yield 93%; ¹H NMR; δ 0.77 (3H, d, *J* = 6.6 Hz), 0.84 (3H, d, *J* = 6.9 Hz), 1.04 (3H, d, *J* = 6.9 Hz), 1.21-1.34 (1H, m), 1.38-1.59 (1H, m), 1.76-2.07 (2H, m), 2.39-2.60 (1H, m), 2.69-2.89 (2H, m), 5.37 (2H, AB, *J* = 17.5 Hz), 7.26-8.00 (10H, m).

Anal. Calcd. for C₂₅H₂₈N₂O: C, 80.61; H, 7.58; N, 7.52. Found: C, 80.54; H, 7.82; N, 7.39.

Volumetric Measurement of Hydrogen Evolution.

In a two necked flask fitted with gas burette, 1-(2'-hydroxyalkyl)-3,5-dimethylpyrazole (0.5 mmol) and appropriate solvent (0.5 ml) was placed. After the injection of borane THF solution (1.0 M, 0.5 ml, 0.5 mmol), volumetric measurement was started. After 1 hour, the reaction mixture was quenched by the injection of methanolic hydrochloric acid (1.0 ml) in order to evaluate the unreacted borane. The result was plotted in Fig. 1 with the data of control experiment in THF.

¹¹B NMR Analysis.

To the THF solution (1.0 ml) of the appropriate pyrazole derivatives (0.5 mmol), borane THF solution (1M, 1.0 ml, 1.0 mmol) was added and stirred for 30 minutes. In the case of **4**, the equimolar mixture of **4** (1.0 mmol) and borane THF solution (1M, 1.0 ml, 1.0 mmol) was used. The mixture was placed in the quart-made NMR tube. ¹¹B NMR spectra were measured by JEOL JNM-EX270 (270 MHz) spectrometer in dry THF with trimethoxyborane as an external standard. ¹¹B NMR spectra of the mixtures of borane-ethanol and borane-triethoxyborane (**7**) were measured as the control experiments, summarized in Table 1.

Borane Reduction of *p*-Methylacetophenone (21**) using *N*-(2'-Hydroxyalkyl)pyrazole.**

Under argon atmosphere, borane THF solution (1M, 0.3 ml, 0.3 mmol) was stirred with *N*-(2'-hydroxyalkyl)pyrazole (0.3 mmol) in hexane (3 ml) for 30 min at room temperature. *p*-Methylacetophenone (**21**, 40 mg, 0.3 mmol) was added and stirred for 24 hours at 80 °C. The mixture was quenched with water and extracted with ether. The organic layer was washed with dilute hydrochloric acid, water, saturated sodium hydrogen carbonate, and saturated sodium chloride, and dried over anhydrous magnesium sulfate. After removal of the solvent, the yields of the products were evaluated by gas chromatography. By the silica gel column chromatography of the residue, the fraction of *p*-methylphenyl-1-ethanol (**22**) was collected and the enantiomer ratio were measured by the gas chromatography using chiral column. The absolute configuration of the product was deduced by the comparison of the optical rotation with authentic data [18].

Detection of 1-(1'-Hydroxypropyl)-3,5-dimethylpyrazole (23**).**

The ¹H NMR of the mixture of propanal (13.9 mg, 0.24 mmol) and 3,5-dimethylpyrazole (18.8 mg, 0.20 mmol) in deuterio chloroform (858 mg) showed the formation of 1-(1'-hydroxypropyl)-3,5-dimethylpyrazole (**23**); ¹H NMR; δ 0.83 (3H, t, *J* = 7.3 Hz), 2.12 (2H, quint, *J* = 7.4 Hz), 2.25 (3H, s), 2.29 (3H, s), 5.41 (1H, t, *J* = 7.1 Hz), 5.80 (1H, s).

Preparation of 1-(1'-Trimethylsiloxyalkyl)-3,5-dimethylpyrazole.

To the THF solution (1 ml) of 3,5-dimethylpyrazole (96 mg, 1 mmol) was added butyllithium hexane solution (1.64 M, 0.61 ml, 1.0 mmol) at -5 °C and stirred for 1 hour. The appropriate aldehyde (1.0 mmol) was added and continued stirring another

1 hour. After the addition of trimethylchlorosilane (0.127 ml, 1.0 mmol), the mixture was stirred for 1 hour at room temperature. The reaction mixture was quenched with saturated sodium hydrogen carbonate and extracted with toluene. The organic layer was washed with water and saturated sodium chloride, dried over anhydrous magnesium sulfate, and concentrated. The residue was purified by silica gel column chromatography with hexane-ethyl acetate mixture.

1-(1'-Trimethylsilyloxypropyl)-3,5-dimethylpyrazole (**24**).

This compound is obtained in yield 72%; bp 100-105 °C/3 mmHg; ¹H NMR; δ 0.03 (9H, s), 0.83 (3H, t, *J* = 7.4 Hz), 2.00 (2H, quint, *J* = 7.4 Hz), 2.20 (3H, s), 2.30 (3H, s), 5.51 (1H, t, *J* = 6.8 Hz), 5.78 (1H, s); ¹³C NMR; δ (DEPT) -0.37 (CH₃), 9.6 (CH₃), 11.4 (CH₃), 13.5 (CH₃), 30.6 (CH₂), 85.2 (CH), 106.4 (CH), 138.4 (C), 147.3 (C); (EI)(m/e, % Int.); 226 (16.1), 211 (53.2), 197 (75.8), 153 (100), 131 (100).

Anal. Calcd. for C₁₁H₂₂N₂OSi: C, 58.36; H, 9.8; N, 12.37. Found: C, 58.38; H, 9.74; N, 12.48.

1-(2'-Methyl-1'-trimethylsilyloxypropyl)-3,5-dimethylpyrazole (**25**).

This compound is obtained in yield 52%; bp 100-110 °C/5 mmHg; ¹H NMR; δ 0.05 (9H, s), 0.66 (3H, d, *J* = 6.8 Hz), 1.00 (1H, m), 1.10 (3H, d, *J* = 6.6 Hz), 2.25 (3H, s), 2.34 (3H, d, *J* = 0.4 Hz), 5.15 (1H, d, *J* = 9.4 Hz), 5.82 (1H, s); ¹³C NMR; δ (DEPT) -0.7 (CH₃), 11.3 (CH₃), 13.3 (CH₃), 17.5 (CH₃), 19.2 (CH₃), 34.9 (CH), 89.0 (CH), 106.0 (CH), 138.1 (C), 146.9 (C).

Anal. Calcd. for C₁₂H₂₄N₂OSi: C, 59.95; H, 10.06; N, 11.65. Found: C, 60.03; H, 10.08; N, 11.49.

1-(1'-Trimethylsilyloxybenzyl)-3,5-dimethylpyrazole (**26**).

This compound is obtained in yield 75%; bp 140-150 °C/5 mmHg; ¹H NMR; δ 0.10 (9H, s), 1.90 (3H, s), 2.23 (3H, s), 5.78 (1H, s), 6.83 (1H, s), 7.29 (5H, s); ¹³C NMR; δ (DEPT) 0.0 (CH₃), 12.1 (CH₃), 14.1 (CH₃), 85.2 (CH), 108.1 (CH), 126.4 (CH), 128.6 (CH), 128.9 (CH), 139.9 (C), 141.3 (C), 147.6 (C).

Anal. Calcd. for C₁₅H₂₂N₂OSi: C, 65.65; H, 8.08; N, 10.21. Found: C, 65.67; H, 8.20; N, 10.42.

1-(1'-Trimethylsilyloxy-2'-phenylpropyl)-3,5-dimethylpyrazole (**27**).

This compound is obtained in yield 73%; bp 145-170 °C/5 mmHg.

Anal. Calcd. for C₁₇H₂₆N₂OSi: C, 67.5; H, 8.66; N, 9.26. Found: C, 67.56; H, 8.66; N, 9.16.

1',2'-syn-Isomer. ¹H NMR; δ 0.25 (9H, s), 1.24 (3H, d, *J* = 7.2 Hz), 2.50 (3H, s), 2.52 (3H, s), 3.67-3.84 (1H, m), 5.73 (1H, d, *J* = 10.4 Hz), 5.75 (1H, s), 7.20-7.56 (5H, m). *1',2'-anti-Isomer.* ¹H NMR; δ 0.26 (9H, s), 1.69 (3H, d, *J* = 7 Hz), 2.05 (3H, s), 2.42 (3H, s), 3.67-3.84 (1H, m), 5.57 (1H, d, *J* = 8.8 Hz), 6.05 (1H, s), 7.20-7.56 (5H, m).

Borane Reduction of *p*-Methylacetophenone (**21**) using *N*-(1'-Hydroxylakyl)pyrazole.

Under an argon atmosphere, 2-benzoyl-3-phenyl-*l*-menthopyrazole (109 mg, 0.31 mmol) was treated with ethylmagnesium

bromide (0.31 mmol) or lithium aluminum hydride (0.31 mmol) in dry ether (3 ml) at -5 °C for 30 min. To the subsequent solution was added borane THF solution (1*M*, 0.3 ml, 0.3 mmol) and stirred at -5 °C for another 30 minutes. After the addition of **21** (0.04 ml, 0.3 mmol), the stirring was continued for 17 hours at -5 °C. The mixture was worked up as describe above.

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