Conjugate Addition of Grignard Reagents to *N*-(α,β-Unsaturated)acylpyrazoles. Diastereoselective β-Alkylation Using 3-Phenyl-*l*-menthopyrazole

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The conjugate additions of *N*-(α,β-unsaturated)acylpyrazoles were carried out by the treatment with Grignard reagents in the presence of cuprous halides. The reaction of 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3a-h** occurred in higher chemical yields and with asymmetric inductions on β-position, where the addition of magnesium bromide as a Lewis acid influenced to the yields and the diastereoselectivities. In the case of α-methylated 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3i-n**, the excellent asymmetric induction on the α-position was also observed through the diastereofacial protonation.

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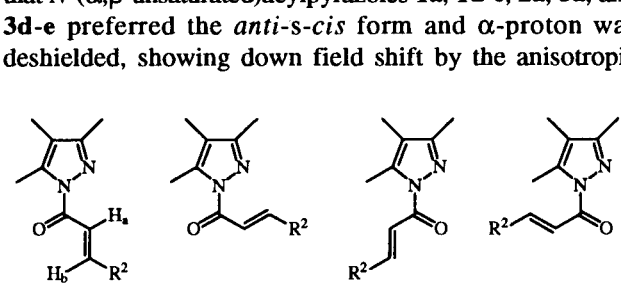
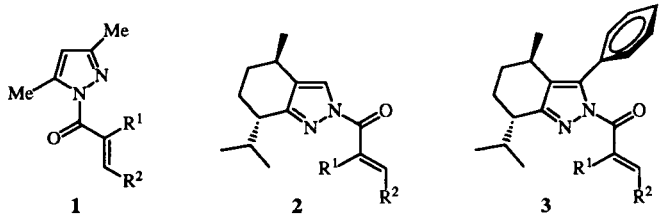
For the synthetic methodology, an auxiliary requires some chemical behavior such as activation of the substrate moiety in substrate-auxiliary intermediates and eventual conversion of the substrate-auxiliary intermediate into the product having the desired functionality. Recently we are very interested in the chemistry of *N*-acylpyrazoles, especially 2-acyl-3-phenyl-*l*-menthopyrazoles, which satisfy the above requirement for an auxiliary [1]. By treatment with various nucleophiles, *N*-acylpyrazoles were converted into the corresponding amides [2], esters [3], ketones [4], and β-keto esters [5]. Moreover the activation by the pyrazole moiety allowed the reaction of *N*-acylpyrazoles with lithium diisopropylamide or lithium hexamethyldisilazide to generate lithium enolates, which were the key intermediates for α-alkylation [6], α-acylation [7], aldolization [8], and α-sulfenylation [9]. In these reactions using 2-acyl-3-phenyl-*l*-menthopyrazoles, the highly selective diastereofacial attack of electrophiles was observed to the lithium enolate, which was rigidly fixed by the intramolecular chelation between lithium and N-1 atom [6]. Also β-sulfenylation was accomplished by the conjugate addition of thiophenol on *N*-(α,β-unsaturated)-acylpyrazoles [9]. Some diastereoselective conjugate additions of the Grignard reagent on the β-position of *N*-(α,β-unsaturated) acid amides were reported using the chiral auxiliaries [10]. In order to extend the utilities of these *N*-acylpyrazoles as the substrate-auxiliary intermediate, a wide variety of the stereoselective reactions of the acyl moiety of *N*-acylpyrazoles are highly desired. Herein, we will describe conjugate addition of carbon nucleophiles to *N*-(α,β-unsaturated)acylpyrazoles for the diastereo controlled introduction of alkyl and aryl groups at the β-position using 3-phenyl-*l*-menthopyrazole as a novel auxiliary.

Results and Discussion.

Generally diastereoselective conjugate addition to α,β-unsaturated carbonyl compounds is known to be dependent on their geometric structure and their facial attack by nucleophiles. Therefore, the geometric structures of *N*-(α,β-unsaturated)acylpyrazoles, especially 2-(α,β-unsaturated)-acyl-3-phenyl-*l*-menthopyrazoles **3** are contrived to be revealed by ^{1}H nmr spectroscopy. From Table 1, the α-proton of α,β-unsaturated acyl groups appeared at 1.3-1.5 ppm lower field than that of α,β-unsaturated acid methyl esters, while the lower shifts less than 0.35 ppm were observed in β-proton peaks. Analogous low field shifts were reported in the cases of α,β-unsaturated phenyl ketones, where α-proton was deshielded by the anisotropic effect of the proximate phenyl group of s-*cis* form [11]. Moreover, the C-N bond between pyrazole ring and acyl carbonyl was previously found to be the *anti* form [12]. These facts suggested that *N*-(α,β-unsaturated)acylpyrazoles **1a**, **1d-e**, **2a**, **3a**, and **3d-e** preferred the *anti*-s-*cis* form and α-proton was deshielded, showing down field shift by the anisotropic



effect of the pyrazole ring. In the cases of *N*-(α-methyl-α,β-unsaturated)acylpyrazoles (**1i-k** and **3i-k**), β-proton signals appeared rather high field compared with those of the corre-



a	R^1 = H, R^2 = Ph	**f**	R^1 = H, R^2 = Et	**k**	R^1 = Me, R^2 = Me
b	R^1 = H, R^2 = *p*-Tol	**g**	R^1 = H, R^2 = *i*-Pr	**m**	R^1 = Me, R^2 = Et
c	R^1 = H, R^2 = *p*-ClC_6H_4	**h**	R^1 = H, R^2 = *t*-Bu	**n**	R^1 = Me, R^2 = *i*-Pr
d	R^1 = H, R^2 = H	**i**	R^1 = Me, R^2 = Ph	**p**	R^1 = Me, R^2 = *t*-Bu
e	R^1 = H, R^2 = Me	**j**	R^1 = Me, R^2 = H		

Table 1
The ^{1}H NMR Data of *N*-Acylpyrazoles

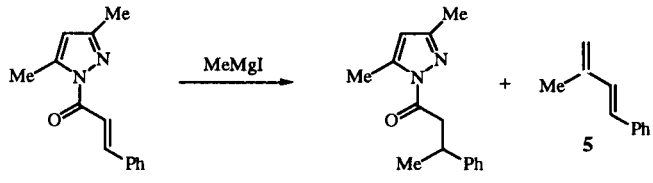
			Acylpyrazole		Me Ester [a]		
	R^1	R^2	Pyrazole	δH_α	δH_β	$\Delta\delta H_\alpha$	$\Delta\delta H_\beta$
1a	H	Ph	3,5-dimethylpyrazolyl-	7.88	7.96	-1.43	-0.26
2a	H	Ph	2-(*l*-menthopyrazolyl)-	7.88	7.98	-1.43	-0.28
3a	H	Ph	2-(3-phenyl-*l*-menthopyrazolyl)-	7.78	8.03	-1.33	-0.33
1d	H	H	3,5-dimethylpyrazolyl-	7.59	6.62	-1.46	-0.20
3d	H	H	2-(3-phenyl-*l*-menthopyrazolyl)-	7.63	6.50	-1.50	-0.08
1e	H	Me	3,5-dimethylpyrazolyl-	7.32	7.20	-1.47	-0.20
3e	H	Me	2-(3-phenyl-*l*-menthopyrazolyl)-	7.33	7.10	-1.48	-0.10
1i	Me	Ph	3,5-dimethylpyrazolyl-		7.33		+0.37
3i	Me	Ph	2-(3-phenyl-*l*-menthopyrazolyl)-		7.30		+0.40
1j	Me	H	3,5-dimethylpyrazolyl-		5.82		+0.25
3j	Me	H	2-(3-phenyl-*l*-menthopyrazolyl)-		5.87		+0.25
1k	Me	Me	3,5-dimethylpyrazolyl-		6.58		+0.27
3k	Me	Me	2-(3-phenyl-*l*-menthopyrazolyl)-		6.53		+0.32

[a] The differences of chemical shifts of methyl esters from those of the corresponding acylpyrazoles; $\Delta\delta = \delta$(Me Ester)-δ(Acylpyrazole).

sponding methyl esters. From this spectral evidence, *N*-(α-methyl-α,β-unsaturated) acylpyrazoles **1i-k** and **3i-k** were also supposed to be preferably the *anti*-s-*trans* form.

The previous paper [12] reported the formation of the chelate complex between *N*-acylpyrazole and magnesium bromide, in which acyl carbonyl group was fixed in the *syn* form. With this background, the Grignard reagent was expected to be a promising carbon nucleophiles for conjugate addition to the *N*-(α,β-unsaturated)acylpyrazoles having the syn-form. By the treatment of 1-cinnamoyl-3,5-dimethylpyrazole (**1a**) with methylmagnesium iodide in tetrahydrofuran, 1-(3-phenyl)butanoyl-3,5-dimethylpyrazole (**4**) was obtained as the desired β-alkylated product accompanied with 3-methyl-1-phenylbutadiene (**5**). The addition of cuprous iodide depressed the formation of the by-product, and the formation of **4** was promoted. Similarly **4** was prepared by the reaction of **1a** with the dimethylcuprate complex, which was prepared *in situ* from cuprous iodide with methyllithium or methylmagnesium iodide.

Scheme 1



1a **4**

When 2-cinnamoyl-3-phenyl-*l*-menthopyrazole (**3a**) was treated with either methylmagnesium iodide in the presence of a cuprous catalyst or the dimethylcuprate complex, the conjugate adduct **6a** was obtained in good yield. The diastereomeric ratio of **6a** was shown to be 5% *de* by integration of the diastereomer 4-methyl peaks of the menthopyrazole group in the ^{1}H nmr [13]. Also the diastereomer ratio was verified by ^{1}H nmr spectroscopy after derivatization into (*S*)-1-(methoxycarbonyl)benzyl ester with removal of the pyrazole moiety by the action of methyl (*S*)-mandelate in the presence of boron trifluoride etherate. Otherwise, the diastereomerically enriched **6a** was hydrolyzed by sodium hydroxide in aqueous methanol, and the absolute configuration of resulting 3-phenylbutanoic acid was determined to be *R*-configuration by comparison with authentic optical rotation data [14]. The diastereoselectivity of this conjugate addition was rationally explained by the *Re*-facial attack of Grignard reagent on the *syn*-s-*cis* form of **3**, which was fixed by the chelation with metal halides such as cuprous iodide and magnesium iodide. Similarly the conjugate addition of phenylmagnesium bromide on 2-crotonoyl-3-phenyl-*l*-menthopyrazoles (**3e**) was performed, and the higher diastereoselectivity with the *S*-configuration on β-position was shown on the formation of **7e** in Table 2.

By the treatment of *N*-acylpyrazoles with excess amount of Lewis acid, the open transition form was expected rather than the cyclic C=O···Mg···N chelated intermediate [13]. Namely, the addition of excess amounts of magnesium bromide allowed to change the geometric structure, and to affect to the diastereoselectivity in the conjugate addition of **3** with Grignard reagents in the presence of cuprous iodide. When 2 equivalents of magnesium bromide were added to the suspension of cuprous iodide in the tetrahydrofuran solution of **3a**, the mixture became a clear orange solution. This homogeneous solution was treated with methylmagnesium iodide to give **6a** in good yield with higher diastereoselectivity of the *S*-configuration on the β-position, listed in Table 2. From Table 2, the yield and the stereoselectivity of **6a** were promoted under the homogeneous conditions using magnesium bromide (runs 2-5) rather than the action of the cuprate complex (runs 11-13), and was independent from the sort of cuprous catalyst

Table 2

Asymmetric Conjugate Addition of 2-(α,β-Unsaturated)acyl-3-phenyl-*l*-menthopyrazole (**3**)

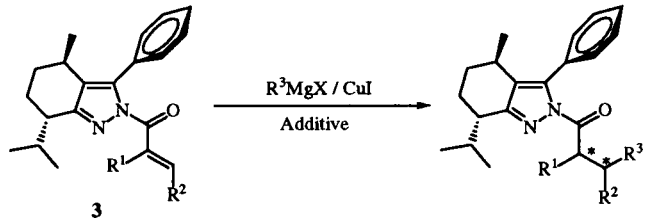
Run		R^2	Nucleophile (equivalents)	Product [a] (Yield %)		De % [b] (configuration)
1	**3a**	Ph	MeMgI (2) + CuI (1)	**6a**	(78)	5 (*R*)
2	**3a**	Ph	MeMgI (2) + CuI (1) + $MgBr_2$ (1)	**6a**	(89)	46 (*S*)
3	**3a**	Ph	MeMgI (2) + CuI (1) + $MgBr_2$(2)	**6a**	(97)	66 (*S*)
4	**3a**	Ph	MeMgI (2) + CuBr (1) + $MgBr_2$(2)	**6a**	(92)	68 (*S*)
5	**3a**	Ph	MeMgI (2) + CuCN (1) + $MgBr_2$ (2)	**6a**	(83)	52 (*S*)
6	**3a**	Ph	MeMgI (2) + CuI (1) + $MgCl_2$ (2)	**6a**	(87)	0
7	**3a**	Ph	MeMgI (2) + CuI (1) + MgI_2 (2)	**6a**	(87)	16 (*S*)
8	**3a**	Ph	MeMgI (2) + CuI (1) + $ZnBr_2$ (2)	**6a**	(79)	16 (*S*)
9	**3a**	Ph	MeMgI (2) + CuI (1) + ZnI_2 (2)	**6a**	(61)	13 (*R*)
10	**3a**	Ph	MeMgI (2) + CuI (1) + Bu_3B (1)	**6a**	(61)	24 (*R*)
11	**3a**	Ph	$Me_2CuMgI{\cdot}MgI_2$ (1) + $MgBr_2$ (2)	**6a**	(80)	29 (*S*)
12	**3a**	Ph	$Me_2CuLi{\cdot}LiI$ (1)	**6a**	(82)	51 (*S*)
13	**3a**	Ph	$Me_2CuLi{\cdot}LiBr{\cdot}Me_2S$ (1)	**6a**	(27)	23 (*S*)
14	**3a**	Ph	EtMgI (2) + CuI (1) + $MgBr_2$ (2)	**8a**	(67)	30 (*S*)
15	**3a**	Ph	*i*-PrMgBr (2) + CuI (1) + $MgBr_2$ (2)	**9a**	(67)	10 (*R*)
16	**3a**	Ph	*t*-BuMgBr (2) + CuI (1) + $MgBr_2$ (2)	**10a**	(53)	6 (*R*)
17	**3b**	*p*-Tol	MeMgI (2) + CuI (1) + $MgBr_2$ (2)	**6b**	(49)	69 (*S*)
18	**3c**	*p*-ClC_6H_4	MeMgI (2) + CuI (1) + $MgBr_2$ (2)	**6c**	(100)	54 (*S*)
19	**3d**	H	PhMgBr (2) + CuBr (1) + $MgBr_2$ (2)	**7d**	(72)	—
20	**3e**	Me	PhMgBr (2) + CuI (1)	**7e**	(75)	80 (*S*)
21	**3e**	Me	PhMgBr (2) + CuI (1) + $MgBr_2$ (2)	**7e**	(96)	49 (*S*)
22	**3e**	Me	*p*-TolMgBr (2) + CuI (1) + $MgBr_2$ (2)	**11e**	(78)	58 (*S*)
23	**3f**	Et	PhMgBr (2) + CuI (1)	**7f**	(63)	70 (*S*)
24	**3f**	Et	PhMgBr (2) + CuBr (1) + $MgBr_2$ (2)	**7f**	(91)	62 (*S*)
25	**3g**	*i*-Pr	PhMgBr (2) + CuI (1)	**7g**	(68)	40 (*R*)
26	**3g**	*i*-Pr	PhMgBr (2) + CuI (1) + $MgBr_2$ (2)	**7g**	(88)	58 (*R*)
27	**3h**	*t*-Bu	PhMgBr (2) + CuI (1)	**7h**	(0)	—
28	**3h**	*t*-Bu	PhMgBr (2) + CuBr (1) + $MgBr_2$ (2)	**7h**	(88)	69 (*R*)

[a] Yields, which were noted in the parentheses, were by hplc. [b] Diastereomer excess (de) values were evaluated by the 4-Me peak of pyrazole moiety in ^1H nmr.

(runs 4-5). A small effect of a Lewis acid was observed by the addition of zinc halides and tributylborane (runs 9-10). The yields and the diastereoselectivities decreased in the reactions with more the bulky Grignard reagents (runs 3 and 14-16). In the case of 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3e-h** other than **3a-c**, the conjugate addition in the presence of magnesium bromide proceeded in satisfactory yields, but *S*-selectivities on the β-position decreased.

Next the asymmetric induction on the α-position was attempted by the conjugate additions of α-methylated 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3i-p** with Grignard reagents. Since the conjugate addition of unsaturated acylpyrazoles was completed by the final protonation of the metal enolate intermediate with an acid, the asymmetric induction on the α-position was dependent on the structure of the metal enolates. When 2-methacryloyl-3-phenyl-*l*-menthopyrazole (**3j**) was treated with Grignard reagents in the presence of cuprous halides, **6j** was formed in good yields with optical yields changing widely as summarized in Table 3. The preferred structure of **6j** was found to be *R*-configuration on the α-position in the short reaction time, whereas *S*-preference was observed by prolonged reaction. This inversion was reasonably interpreted by slow conversion into the *Z*-enolate from the *E*-enolate, which was first formed by the conjugate addition of Grignard reagent on s-*trans* form of **3j**. In the case of **3k**, the metal enolate was rapidly isomerized into the thermally stable *Z*-enolate, and subsequent protonation from

Scheme 2



3

a R^1 = H, R^2 = Ph
b R^1 = H, R^2 = *p*-Tol
c R^1 = H, R^2 = *p*-ClC_6H_4
d R^1 = H, R^2 = H
e R^1 = H, R^2 = Me
f R^1 = H, R^2 = Et
g R^1 = H, R^2 = *i*-Pr
h R^1 = H, R^2 = *t*-Bu
i R^1 = Me, R^2 = Ph
j R^1 = Me, R^2 = H
k R^1 = Me, R^2 = Me
m R^1 = Me, R^2 = Et
n R^1 = Me, R^2 = *i*-Pr
p R^1 = Me, R^2 = *t*-Bu

6 R^3 = Me
7 R^3 = Ph
8 R^3 = Et
9 R^3 = *i*-Pr
10 R^3 = *t*-Bu
11 R^3 = p-Tol

Table 3

Asymmetric Induction at α-Position on the Conjugate Addition to 2-(α-Methyl-α,β-Unsaturated)acyl-3-phenyl-*l*-menthopyrazole (**3**)

Run		R^2	Nucleophile (equiv.)	Time (h)	Product [a] (Yield %)	De % [b] (configuration)
1	**3i**	Ph	PhMgBr (1) + CuI (1)	3	**7i** (18)	87 (S)
2	**3i**	Ph	PhMgBr (1) + CuI (1) + $MgBr_2$(2)	2	**7i** (54)	97 (S)
3	**3j**	H	MeMgI (1) + CuI (1)	2	**6j** (70)	47 (R)
4	**3j**	H	MeMgI (1) + CuI (1)	12	**6j** (25)	22 (S)
5	**3j**	H	MeMgI (1) + CuI (1) + $MgBr_2$(2)	12	**6j** (70)	6 (S)
6	**3j**	H	PhMgBr (1) + CuI (1)	2	**7j** (71)	0
7	**3k**	Me	MeMgI (1) + CuBr(1)	2	**6k** (74)	88 (S)
8	**3k**	Me	MeMgI (1) + CuI(1)	12	**6k** (75)	78 (S)
9	**3k**	Me	MeMgI (1) + CuBr (1) + $MgBr_2$(2)	2	**6k** (77)	78 (S)

[a] Yields, which were noted in the parentheses, were evaluated by hplc. [b] Diastereomer excess (de) values were evaluated by the 4-Me peak of pyrazole moiety in the ^1H nmr spectra.

the *re*-face afforded the conjugate adduct **6k** with *S*-configuration on the α-position. Similarly a very high diastereoselectivity on the α-position was observed in the reaction of **3i** with phenylmagnesium bromide.

Finally the conjugate additions of **3i-p** with Grignard reagents were performed for the double asymmetric induction on the α- and β-positions. The treatment of **3k** with phenylmagnesium bromide in the presence of cuprous halide afforded (2'*S*,3'*S*)-2-(2'-methyl-3'-phenyl)butanoyl-3-phenyl-*l*-menthopyrazole (**7k**) with excellent diastereoselectivities on either the α- and β-position. The stereo structure of **7k** was supported by the derivatization into (2*S*,3*S*)-2-(2-methyl-3-phenyl)butanoic acid. Similar asymmetric induction on α- and β-position was simultaneously accomplished by the conjugate addition of **3m** and **3n** summarized in Table 4. In the case of **3i** with methylmagnesium iodide, excellent diastereoselectivity of the α-position was observed with a low *R*-selectivity on the β-position. By the addition of magnesium bromide, the selectivity on the β-position was reversed like the conjugate addition to **3a**.

In conclusion, the conjugate additions of *N*-(α,β-unsaturated)acylpyrazoles were carried out by the treatment with

Scheme 3

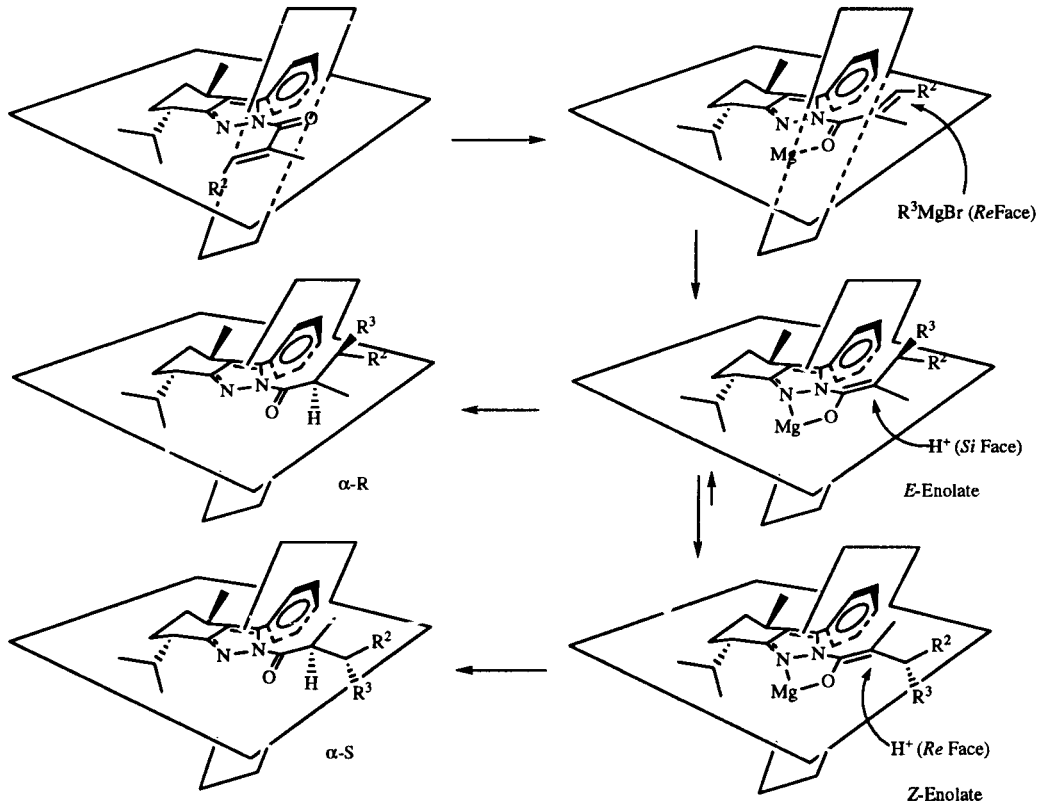


Table 4

Double Asymmetric Induction at α- and β-Positions on the Conjugate Addition to 2-(α-Methyl-α,β-Unsaturated)acyl-3-phenyl-*l*-menthopyrazole (3)

Run	Substrate		Nucleophile (equivalent)	Product [a] (Yield %)		De % (configuration) [b]	
		R^2				α-Position	β-Position
1	**3i**	Ph	MeMgI (1) + CuI (1)	**6i** (70)	>95 (*S*)	30	(*R*)
2	**3i**	Ph	MeMgI (1) + CuI (1) + $MgBr_2$ (2)	**6i** (25)	>95 (*S*)	20	(*S*)
3	**3k**	Me	PhMgBr (1) + CuI (1)	**7k** (84)	>95 (*S*)	92	(*S*)
4	**3k**	Me	PhMgBr (1) + CuBr (1) + $MgBr_2$ (2)	**7k** (56)	>95 (*S*)	88	(*S*)
5	**3m**	Et	PhMgBr (1) + CuI (1)	**7m** (82)	>95 (*S*)	79	(*S*)
6	**3m**	Et	PhMgBr (1) + CuBr (1) + $MgBr_2$ (2)	**7m** (63)	>95 (*S*)	92	(*S*)
7	**3n**	*i*-Pr	PhMgBr (1) + CuI (1)	**7n** (0)	—	—	
8	**3n**	*i*-Pr	PhMgBr (1) + CuI (1) + $MgBr_2$ (2)	**7n** (26)	>95 (*S*)	63	(*S*)
9	**3p**	*t*-Bu	PhMgBr (1) + CuI (1)	**7p** (0)	—	—	
10	**3p**	*t*-Bu	PhMgBr (1) + CuI (1) + $MgBr_2$ (2)	**7p** (0)	—	—	

[a] Yields, which were noted in the parentheses, were evaluated by hplc. [b] Diastereomer excess (de) values were evaluated by the 4-Me peak of pyrazole moiety in the ^1H nmr spectra.

Grignard reagents in the presence of cuprous halides. The reaction of 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3a-h** occurred in a high chemical yield with high asymmetric induction on its β-position, whereas the addition of magnesium bromide as a Lewis acid influenced the yields and the diastereoselectivities. In the case of α-methylated 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3i-n**, the asymmetric induction on the α-position was also observed with excellent selectivity through the diastereofacial protonation. Especially, the treatment of 2-(2-methyl-2-butenoyl)-3-phenyl-*l*-menthopyrazole (**3k**) with phenylmagnesium bromide afforded (2'*S*,3'*S*)-2-(2'-methyl-3'-phenyl)butanoyl-3-phenyl-*l*-menthopyrazole (**7k**) with excellent diastereoselectivities on both the α-and β-positions. This asymmetric induction was dependent on the preferable structure of *N*-(α,β-unsaturated)acylpyrazoles and the intermediate magnesium enolates, which were elucidated by ^1H nmr spectroscopy.

EXPERIMENTAL

Melting points are uncorrected. The ^1H nmr and ^{13}C nmr spectra were obtained on JEOL JNM-EX270 (270 MHz) spectrometers in deuterochloroform 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.

Materials.

Tetrahydrofuran and ether were dried over benzophenone ketyl radical. 4,4-Dimethyl-2-pentenoic acid [16], 2,4,4-trimethyl-2-pentenoic acid [16], 4-methyl-2-pentenoic acid [17], and 2,4-dimethyl-2-pentenoic acid [17] were prepared by the usual methods. These α,β-unsaturated acids were applicable for the preparation of 1-(α,β-unsaturated)acyl-3,5-dimethylpyrazoles **1** and 2-(α,β-unsaturated)acyl-3-phenyl-*l*-menthopyrazoles **3** according to the method reported in the previous papers [3], [6]. Magnesium bromide etherate was commercially available from Aldrich Chemicals Co.

2-Cinnamoyl-3-phenyl-*l*-menthopyrazole (**3a**).

This compound had mp 79.5-80.5° (from methanol); yield 51%; ^1H nmr: δ 0.71 (3H, d, J = 7 Hz), 0.97 (3H, d, J = 7 Hz), 1.12 (3H, d, J = 7 Hz), 1.19-1.31 (1H, m), 1.47-1.59 (1H, m), 1.84-1.98 (2H, m), 2.46-2.58 (1H, m), 2.65-2.81 (2H, m), 7.31-7.59 (10H, m), 7.80 (1H, d, J = 16 Hz), 7.99 (1H, d, J = 16 Hz).

Anal. Calcd. for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29. Found: C, 81.19; H, 7.37; N, 7.31.

2-(*p*-Methylcinnamoyl)-3-phenyl-*l*-menthopyrazole (**3b**).

This compound was obtained in a yield of 51%; ^1H nmr: δ 0.72 (3H, d, J = 7 Hz), 0.96 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 7 Hz), 1.16-1.31 (1H, m), 1.47-1.59 (1H, m), 1.84-1.98 (2H, m), 2.33 (3H, s), 2.49-2.55 (1H, m), 2.65-2.81 (2H, m), 7.14 (2H, d, J = 8 Hz), 7.28-7.43 (5H, m), 7.48 (2H, d, J = 8 Hz), 7.78 (1H, AB, J = 16 Hz), 7.94 (1H, AB, J = 16 Hz).

Anal. Calcd. for $C_{27}H_{30}N_2O$: C, 81.37; H, 7.59; N, 7.03. Found: C, 81.32; H, 7.66; N, 7.13.

2-(*p*-Chlorocinnamoyl)-3-phenyl-*l*-menthopyrazole (**3c**).

This compound was obtained in a yield of 65%; ^1H nmr: δ 0.73 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.12 (3H, d, J = 7 Hz), 1 21-1.33 (1H, m), 1.49-1.61 (1H, m), 1.89-2.01 (2H, m), 2.47-2.54 (1H, m), 2.65-2.83 (2H, m), 7.26-7.55 (5H, m), 7.72 (1H, AB, J = 16 Hz), 7.92 (1H, AB, J = 16 Hz).

Anal. Calcd. for $C_{26}H_{27}N_2OCl$: C, 74.54; H, 6.5; N, 6.69. Found: C, 74.71; H, 6.53; N, 6.72.

2-Acryl-3-phenyl-*l*-menthopyrazole (**3d**).

This compound was obtained in a yield of 46%; ^1H nmr: δ 0.71 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.19-1.32 (1H, m), 1.46-1.59 (1H, m), 1.84-1.98 (2H, m), 2.41-2.48 (1H, m), 2.61-2.69 (1H, m), 2.73-2.81 (1H, m), 5.88 (1H, d-d, J = 10, 1 Hz), 6.50 (1H, d-d, J = 17, 1 Hz), 7.30-7.42 (5H, m), 7.63 (1H, d-d, J = 17, 10 Hz).

Anal. Calcd. for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 78.03; H, 7.92; N, 9.05.

2-Crotonoyl-3-phenyl-*l*-menthopyrazole (**3e**).

This compound was obtained in a yield of 52%; ^1H nmr: δ 0.71 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 1.10 (3H, d, J = 7 Hz), 1.20-1.32 (1H, m), 1.47-1.61 (1H, m), 1.84-2.03 (5H, m), 2.40-

2.52 (1H, m), 2.62-2.80 (2H, m), 7.02-7.15 (2H, m), 7.24-7.42 (5H, m).

Anal. Calcd. for $C_{21}H_{26}N_2O$: C, 78.22; H, 8.13; N, 8.69. Found: C, 78.37; H, 8.19; N, 8.70.

2-(2'-Pentenoyl)-3-phenyl-*l*-menthopyrazole (**3f**).

This compound was obtained in a yield of 53%; ^{1}H nmr: δ 0.71 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.08 (3H, t, J = 7 Hz), 1.11 (3H, d, J = 7 Hz), 1.17-1.31 (1H, m), 1.46-1.59 (1H, m), 1.83-1.96 (2H, m), 2.23-2.34 (2H, m), 2.43-2.50 (1H, m), 2.62-2.79 (2H, m), 7.13 (1H, d-t, J = 7, 16 Hz), 7.29-7.41 (6H, m).

Anal. Calcd. for $C_{22}H_{28}N_2O$: C, 78.53; H, 8.39; N, 8.33. Found: C, 78.58; H, 8.46; N, 8.28.

2-(4'-Methyl-2'-pentenoyl)-3-phenyl-*l*-menthopyrazole (**3g**).

This compound was obtained in a yield of 42%; ^{1}H nmr: δ 0.71 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.06-1.11 (9H, m), 1.18-1.32 (1H, m), 1.46-1.59 (1H, m), 1.84-1.98 (2H, m), 2.40-2.80 (4H, m), 7.05 (1H, d-d, J = 7, 16 Hz), 7.26 (1H, d-d, J = 1, 16 Hz), 7.29-7.43 (m, 5H).

Anal. Calcd. for $C_{23}H_{30}N_2O$: C, 78.82; H, 8.63; N, 7.99. Found: C, 78.98; H, 8.80; N, 7.85.

2-(4',4'-Dimethyl-2'-pentenoyl)-3-phenyl-*l*-menthopyrazole (**3h**).

This compound was obtained in a yield of 63%; ^{1}H nmr: δ 0.71 (3H, d, J = 7 Hz), 0.97 (3H, d, J = 7 Hz), 1.08-1.12 (12H, m), 1.14-1.34 (1H, m), 1.47-1.59 (1H, m), 1.86-1.98 (2H, m), 2.39-2.48 (1H, m), 2.62-2.80 (2H, m), 7.10 (1H, AB, J = 16 Hz), 7.26 (1H, AB, J = 16 Hz), 7.17-7.41 (5H, m).

Anal. Calcd. for $C_{24}H_{32}N_2O$: C, 79.08; H, 8.85; N, 7.68. Found: C, 79.0; H, 8.97; N, 7.67.

2-(2'-Methylcinnamoyl)-3-phenyl-*l*-menthopyrazole (**3i**).

This compound was obtained in a yield of 63%; ^{1}H nmr: δ 0.78 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 1.07 (3H, d, J = 7 Hz), 1.20-1.32 (1H, m), 1.46-1.55 (1H, m), 1.85-1.97 (2H, m), 2.21 (3H, d, J = 1 Hz), 2.44-2.51 (1H, m), 2.64-2.72 (1H, m), 2.77-2.85 (1H, m), 7.15-7.36 (10H, m).

Anal. Calcd. for $C_{27}H_{30}N_2O$: C, 81.37; H, 7.59; N, 7.03. Found: C, 81.26; H, 7.70; N, 7.04.

2-Methacryloyl-3-phenyl-*l*-menthopyrazole (**3j**).

This compound was obtained in a yield of 50%; ^{1}H nmr: δ 0.75 (3H, d, J = 7 Hz), 0.91 (3H, d, J = 7 Hz), 1.06 (3H, d, J = 7 Hz), 1.19-1.31 (1H, m), 1.46-1.58 (1H, m), 1.83-1.99 (2H, m), 2.08 (3H, s), 2.40-2.47 (1H, m), 2.62-2.69 (1H, m), 2.75-2.83 (1H, m), 5.66 (1H, t, J = 1 Hz), 5.86 (1H, s), 7.29-7.40 (5H, m).

Anal. Calcd. for $C_{21}H_{26}N_2O$: C, 78.22; H, 8.13; N, 8.69. Found: C, 78.07; H, 8.23; N, 8.58.

2-(2'-Methylcrotonoyl)-3-phenyl-*l*-menthopyrazole (**3k**).

This compound was obtained in a yield of 56%; ^{1}H nmr: δ 0.77 (3H, d, J = 7 Hz), 0.89 (3H, d, J = 7 Hz), 1.06 (3H, d, J = 7 Hz), 1.20-1.33 (1H, m), 1.49-1.58 (1H, m), 1.78 (3H, d-d, J = 7, 1 Hz), 1.82-1.98 (2H, m), 1.92 (3H, t, J = 1 Hz), 2.42-2.49 (1H, m), 2.63-2.70 (1H, m), 2.76-2.84 (1H, m), 6.53 (1H, d-q, J = 7, 1 Hz), 7.28-7.40 (5H, m).

Anal. Calcd. for $C_{22}H_{28}N_2O$: C, 78.53; H, 8.39; N, 8.33. Found: C, 78.33; H, 8.45; N, 8.34.

2-(2'-Methyl-2'-pentenoyl)-3-phenyl-*l*-menthopyrazole (**3m**).

This compound was obtained in a yield of 60%; ^{1}H nmr: δ 0.77 (3H, d, J = 7 Hz), 0.91 (3H, d, J = 7 Hz), 1.01 (3H, t, J = 7 Hz), 1.07 (3H, d, J = 7 Hz), 1.21-1.33 (1H, m), 1.46-1.59 (1H, m), 1.83-2.00 (2H, m), 1.91 (3H, d, J = 1 Hz), 2.13-2.25 (2H, m), 2.37-2.47 (1H, m), 2.63-2.70 (1H, m), 2.76-2.84 (1H, m), 6.40 (1H, d-t, J = 1, 7 Hz), 7.24-7.40 (5H, m).

Anal. Calcd. for $C_{23}H_{30}N_2O$: C, 78.82; H, 8.63; N, 7.99. Found: C, 78.84; H, 8.76; N, 7.92.

2-(2',4'-Dimethyl-2'-pentenoyl)-3-phenyl-*l*-menthopyrazole (**3n**).

This compound was obtained in a yield of 46%; ^{1}H nmr: δ 0.77 (3H, d, J = 7 Hz), 0.95 (6H, d, J = 7 Hz), 1.02 (3H, d, J = 7 Hz), 1.08 (3H, d, J = 7 Hz), 1.13-1.33 (1H, m), 1.46-1.59 (1H, m), 1.85-2.06 (2H, m), 1.93 (3H, d, J = 1 Hz), 2.36-2.48 (1H, m), 2.58-2.71 (2H, m), 2.73-2.84 (1H, m), 6.21 (1H, d-d, J = 1, 10 Hz), 7.29-7.38 (5H, m).

Anal. Calcd. for $C_{24}H_{32}N_2O$: C, 79.08; H, 8.85; N, 7.68. Found: C, 78.93; H, 9.02; N, 7.52.

2-(2',4',4'-Trimethyl-2'-pentenoyl)-3-phenyl-*l*-menthopyrazole (**3p**).

This compound was obtained in a yield of 42% ; ^{1}H nmr: δ 0.76 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.08 (3H, d, J = 7 Hz), 1.11 (9H, s), 1.14-1.39 (1H, m), 1.46-1.64 (1H, m), 1.83-2.14 (2H, m), 2.01 (3H, d, J = 1 Hz), 2.39-2.45 (1H, m), 2.63-2.70 (1H, m), 2.76-2.83 (1H, m), 6.22 (1H, d, J = 1 Hz), 7.21-7.38 (5H, m).

Anal. Calcd. for $C_{25}H_{34}N_2O$: C, 79.32; H, 9.05; N, 7.4. Found: C, 79.32; H, 9.16; N, 7.43.

2-Cinnamoyl-*l*-menthopyrazole (**2a**).

This compound was obtained in a yield of 46%; ^{1}H nmr: δ 0.94 (3H, d, J = 7 Hz), 1.10 (3H, d, J = 7 Hz), 1.21 (3H, d, J = 7 Hz), 1.45-1.59 (1H, m), 1.68-1.98 (3H, m), 2.25-2.38 (1H, m), 2.62-2.68 (1H, m), 2.81-2.88 (1H, m), 7.33-7.43 (3H, m), 7.59-7.70 (2H, m), 7.93 (2H, AB-q, J = 16 Hz), 8.08 (1H, d, J =0.7 Hz).

Anal. Calcd. for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.51; H, 7.56; N, 9.02.

General Procedure for the Conjugate Addition of *N*-Acylpyrazoles.

With R^3MgX.

To a suspension of *N*-(α,β-unsaturated)acylpyrazole **1** or **3** (0.5 mmole) and cuprous halide (0.55 mmole) in tetrahydrofuran (2.5 ml), 0.5 ml of Grignard reagent (2.0 M in ether) was added dropwise at -78°, and the mixture stirred for another 2 hours at room temperature. The reaction mixture was quenched with acetic acid and water, cuprous salt was filtered through Celite (No. 545), and the products were extracted with dichloromethane. The organic layer was washed with dilute hydrochloric acid, water, saturated sodium hydrogen carbonate, and sodium chloride. After dried over anhydrous magnesium sulfate, the solvent was removed under reduced pressure. The residue was chromatographed on silica gel with hexane-benzene (1:1 v/v) mixture.

With Grignard Reagent-Magnesium Bromide.

To a suspension of *N*-(α,β-unsaturated)acylpyrazole **1** or **3** (0.5 mmole) and cuprous halide (0.55 mmole) in tetrahydrofuran (2.5 ml), 5.0 ml of anhydrous magnesium bromide solution (0.2 *M* in tetrahydrofuran) was added under a nitrogen atmosphere at room temperature. During 10 minutes stirring at room temperature, the mixture changed into a clear orange solution. To this solution, 0.5 ml of Grignard reagent (2.0 *M* in ether) was added dropwise at

-78°, and stirred for another 2 hours at room temperature. The mixture was worked up as describe above.

With Lithium Dimethylcuprate.

To the suspension of cuprous iodide (0.32 mmole) in ether (2 ml) was gradually added 0.5 ml of methyllithium (1.2 *M* in ether) at -78°, and stirring was continued for 30 minutes at -20°. The solution was chilled at -78° and was treated with *N*-(α,β-unsaturated)acylpyrazole **1** or **3** (0.3 mmole) in ether (1 ml). After 2 hours stirring at room temperature, the mixture was worked up as describe above.

1-(3'-Phenylbutanoyl)-3,5-dimethylpyrazole (**4a**).

This compound had bp 190°/5 mm Hg, yield 99%; ^{1}H nmr: δ 1.35 (3H, d, J = 7 Hz), 2.22 (3H, s), 2.48 (3H, s), 3.29-3.51 (3H, m), 5.92 (1H, s), 7.14-7.30 (5H, m).

Anal. Calcd. for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.08; H, 7.45; N, 11.46.

1-Phenyl-3-methyl-1,3-butadiene (**5a**).

This compound was obtained in a yield of 31%; ^{1}H nmr: δ 1.96 (3H, d, J = 1.7 Hz), 5.06 (1H, s), 5.11 (1H, s), 6.52 (1H, d-d, J = 2.6, 16.2 Hz), 6.87 (1H, d-d, J = 3, 16 Hz), 7.17-7.23 (1H, m), 7.26-7.33 (2H, m), 7.39-7.42 (2H, m).

2-(3'-Phenylbutanoyl)-3-phenyl-*l*-menthopyrazole **6a** or **7e**.

This compound had bp 195-200°/5 mm Hg, yield 67%.

Anal. Calcd. for $C_{27}H_{32}N_2O$: C, 80.96; H, 8.05; N, 6.99; Found: C, 81.14; H, 8.08; N, 7.08.

3'*R*-Isomer.

This compound had ^{1}H nmr: δ 0.69 (3H, d, J = 7 Hz), 0.93 (3H, d, J = 7 Hz),1.09 (3H, d, J = 7 Hz), 1.31 (3H, d, J = 7 Hz), 1.20-1.54 (2H, m), 1.84-1.96 (2H, m), 2.40-2.47 (1H, m), 2.60-2.77 (2H, m), 3.20-3.57 (3H, m), 7.14-7.40 (10H, m).

3'*S*-Isomer.

This compound had ^{1}H nmr: δ 0.67 (3H, d, J = 7 Hz), 0.96 (3H, d, J = 7 Hz),1.10 (3H, d, J = 7 Hz), 1.30 (3H, d, J = 7 Hz), 1.20-1.54 (2H, m), 1.84-1.96 (2H, m), 2.40-2.47 (1H, m), 2.60-2.77 (2H, m), 3.20-3.57 (3H, m), 7.14-7.40 (10H, m).

(3'*S*)-2-[(3'-*p*-Methylphenyl)butanoyl]-3-phenyl-*l*-menthopyrazole **6b** or **11e**.

This compound was obtained in a yield of 49%; ^{1}H nmr: δ 0.67 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.15-1.30 (1H, m), 1.28 (3H, d, J = 7 Hz), 1.45-1.58 (1H, m), 1.82-1.99 (2H, m), 2.31 (3H, s), 2.37-2.46 (1H, m), 2.58-2.65 (1H, m), 2.71-2.78 (1H, m), 3.22-3.46 (3H, m), 7.08-7.39 (9H, m).

Anal. Calcd. for $C_{28}H_{34}N_2O$: C, 81.12; H, 8.27; N, 6.76. Found: C, 80.87; H, 8.28; N, 6.81.

(3'*S*)-2-[(3'-*p*-Chlorophenyl)butanoyl]-3-phenyl-*l*-menthopyrazole (**6c**).

This compound was obtained in a yield of 100%; ^{1}H nmr: δ 0.67 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.13-1.29 (1H, m), 1.25 (3H, d, J = 7 Hz), 1.44-1.57 (1H, m), 1.82-1.96 (2H, m), 2.37-2.49 (1H, m), 2.57-2.65 (1H, m), 2.70-2.78 (1H, m), 3.15-3.55 (3H, m), 7.13-7.39 (9H, m).

Anal. Calcd. for $C_{27}H_{31}N_2OCl$: C, 74.55: H, 7.18; N, 6.44. Found: C, 74.56; H, 7.44; N, 6.42.

2-(2'-Methylbutanoyl)-3-phenyl-*l*-menthopyrazole (**6j**).

This compound had ^{13}C nmr: δ (DEPT) 11.5 (CH_3), 16.5 (CH_3), 18.6 (CH_3), 20.2 (CH_3), 23.2 (CH_2), 27.1 (CH_2), 27.4 (CH), 30.0 (CH), 32.3 (CH_2), 39.4 (CH), 41.4 (CH), 126.0 (C), 127.8 (CH), 128.0 (CH), 129.2 (CH), 132.8 (C), 140.8 (C), 155.3 (C), 176.7 (C).

Anal. Calcd. for $C_{22}H_{30}N_2O$: C, 78.06; H, 8.93; N, 8.28. Found: C, 77.75; H, 8.83; N, 8.24.

2'*R*-Isomer.

This compound had ^{1}H nmr: δ 0.70 (3H, d, J = 7 Hz), 0.88 (3H, t, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.21 (3H, d, J = 7 Hz), 1.43-1.53 (2H, m), 1.58-1.81 (2H, m), 1.84-2.03 (2H, m), 2.35-2.48 (1H, m), 2.60-2.83 (2H, m), 3.86 (1H, sex, J = 7 Hz), 7.20-7.42 (5H, m).

2'*S*-Isomer.

This compound had ^{1}H nmr: δ 0.69 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 0.96 (3H, t, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.17 (3H, d, J = 7 Hz), 1.20-1.31 (1H, m), 1.42-1.64 (2H, m), 1.66-2.04 (3H, m), 2.35-2.47 (1H, m), 2.60-2.67 (1H, m), 2.69-2.86 (1H, m), 3.60 (1H, sex, J = 7 Hz), 7.25-7.46 (5H, m).

2-(2',3'-Dimethylbutanoyl)-3-phenyl-*l*-menthopyrazole (**6k**).

This compound had bp 123°/2 mm Hg, yield 78%.

Anal. Calcd. for $C_{23}H_{32}N_2O$: C, 78.36; H, 9.15; N, 7.95. Found: C, 78.36; H, 9.38; N, 8.06.

2'*R*-Isomer.

This compound had ^{1}H nmr: δ 0.70 (3H, d, J = 7 Hz), 0.87 (3H, d, J = 7 Hz), 0.89 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.14 (3H, d, J = 7 Hz), 1.20 (2H, m), 1.51 (1H, m), 1.95 (2H, m), 2.43 (1H, m), 2.65 (1H, m), 2.74 (1H, m), 3.81 (1H, quint, J = 7 Hz), 7.37 (5H, m).

2'*S*-Isomer.

This compound had ^{1}H nmr: δ 0.68 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 0.99 (3H, d, J = 7 Hz), 1.08 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 7 Hz), 1.15-1.31 (1H, m), 1.44-1.57 (1H, m), 1.80-2.00 (2H, m), 2.05-2.17 (1H, m), 2.35-2.47 (1H, m), 2.59-2.73 (1H, m), 2.76-2.81 (1H, m), 3.72 (1H, quint, J = 7 Hz), 7.22-7.42 (5H, m).

2-(3',3'-Diphenylpropanoyl)-3-phenyl-*l*-menthopyrazole (**7a**).

This compound was obtained in a yield of 75%; ^{1}H nmr: δ 0.66 (3H, d, J = 7 Hz), 0.96 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 7 Hz), 1.21-1.30 (1H, m), 1.45-1.53 (1H, m), 1.86-1.95 (2H, m), 2.46-2.52 (1H, m), 2.63-2.73 (2H, m), 3.71-3.81 (1H, m), 3.96-4.05 (1H, m), 4.72-4.77 (1H, m), 7.05-7.34 (15H, m).

Anal. Calcd. for $C_{32}H_{34}N_2O$: C, 83.08; H, 7.41; N, 6.06. Found: C, 83.04; H, 7.27; N, 6.09.

2-(3'-Phenylpropanoyl)-3-phenyl-*l*-menthopyrazole (**7d**).

This compound had bp 135°/2 mm Hg, yield 86%; ^{1}H nmr: δ 0.69 (3H, d, J = 7 Hz), 0.92 (3H, d, J = 7 Hz), 1.07 (3H, d, J = 7 Hz), 1.24 (1H, q, J = 7 Hz), 1.52 (1H, m), 1.91 (2H, m), 2.40 (1H, m), 2.61 (1H, m), 2.74 (1H, m), 3.00 (2H, t, J = 7 Hz), 3.43 (2H, m), 7.36 (10H, m).

Anal. Calcd. for $C_{26}H_{30}N_2O$: C, 80.79; H, 7.82; N, 7.25. Found: C, 80.75; H, 8.07; N, 7.36.

(3'*S*)-2-(3'-Phenylpentanoyl)-3-phenyl-*l*-menthopyrazole **7f** or **8a**.

This compound was obtained in a yield of 91% from **3f**; ^{1}H nmr: δ 0.66 (3H, d, J = 7 Hz), 0.76 (3H, t, J = 7 Hz), 0.96 (3H, d, J = 7 Hz), 1.10 (3H, d, J = 7 Hz), 1.16-1.28 (1H, m), 1.45-1.95 (5H, m), 2.41-2.48 (1H, m), 2.59-2.78 (2H, m), 3.15-3.23 (1H, m), 3.28-3.50 (2H, m), 7.10-7.33 (10H, m).

Anal. Calcd. for $C_{28}H_{34}N_2O$: C, 81.12; H, 8.27; N, 6.76. Found: C, 80.89; H, 8.33; N, 6.52.

(3'*S*)-2-(4'-Methyl-3'-phenylpentanoyl)-3-phenyl-*l*-menthopyrazole **7g** or **9a**.

This compound was obtained in a yield of 88% (from **3g**); ^{1}H nmr: δ 0.65 (3H, d, J = 7 Hz), 0.76 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 0.97 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 7 Hz), 1.15-1.28 (1H, m), 1.44-1.57 (1H, m), 1.82-1.96 (3H, m), 2.44-2.52 (1H, m), 2.60-2.76 (2H, m), 3.06-3.14 (1H, m), 3.32-3.42 (1H, m), 3.58-3.66 (1H, m), 6.96-7.05 (2H, m), 7.11-7.35 (8H, m).

Anal. Calcd. for $C_{29}H_{36}N_2O$: C, 81.27; H, 8.47; N, 6.54. Found: C, 81.27; H, 8.56; N, 6.54.

(3'*S*)-2-(4',4'-Dimethyl-3'-phenylpentanoyl)-3-phenyl-*l*-menthopyrazole (**7h** or **10a**).

This compound was obtained in a yield of 88% (from **3h**); ^{1}H nmr: δ 0.65 (3H, d, J = 7 Hz), 0.91 (9H, s), 0.99 (3H, d, J = 7 Hz), 1.13 (3H, d, J = 7 Hz), 1.19-1.27 (1H, m), 1.48-1.53 (1H, m), 1.83-1.93 (2H, m), 2.47-2.54 (1H, m), 2.61-2.74 (2H, m), 3.18-3.28 (1H, m), 3.46-3.59 (2H, m), 6.83-6.87 (2H, m), 7.12-7.86 (8H, m).

Anal. Calcd. for $C_{30}H_{38}N_2O$: C, 81.4; H, 8.65; N, 6.33. Found: C, 81.63; H, 8.54; N, 5.94.

(2'*S*)-2-(2'-Methyl-3',3'-diphenylpropanoyl)-3-phenyl-*l*-menthopyrazole (**7i**).

This compound was obtained in a yield of 54%; ^{1}H nmr: δ 0.63 (3H, d, J = 7 Hz), 0.93 (3H, d, J = 7 Hz), 1.10 (3H, d, J = 7 Hz), 1.16 (3H, d, J = 7 Hz), 1.24 (1H, q, J = 11 Hz), 1.52 (1H, q, J = 10 Hz), 1.84-2.00 (2H, m), 2.41-2.52 (1H, m), 2.65-2.83 (2H, m), 4.23 (1H, d, J = 12 Hz), 4.78-4.90 (1H, m), 6.72 (2H, d, J = 7 Hz), 7.01-7.56 (13H, m).

Anal. Calcd. for $C_{33}H_{36}N_2O$: C, 83.15; H, 7.61; N, 5.88. Found: C, 82.96; H, 7.53; N, 5.85.

(2'*R*)-2-(2'-Methyl-3'-phenylpropanoyl)-3-phenyl-*l*-menthopyrazole (**7j**).

This compound had bp 135°/2 mm Hg, yield 72%; ^{1}H nmr: δ 0.70 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 1.10 (3H, d, J = 7 Hz), 1.17 (3H, d, J = 7 Hz), 1.20 (1H, m), 1.16 (1H, m), 1.93 (2H, m), 2.47 (1H, m), 2.54-2.74 (3H, m), 3.14 (1H, d-d, J = 6, 13 Hz), 4.25 (1H, sext, J = 7 Hz), 7.36 (10H, m).

Anal. Calcd. for $C_{27}H_{32}N_2O$: C, 80.96; H, 8.05; N, 6.99. Found: C, 81.03; H, 8.15; N, 6.70.

(2'*S*,3'*S*)-2-(2'-Methyl-3'-phenylbutanoyl)-3-phenyl-*l*-menthopyrazole **6i** or **7k**.

This compound was obtained in a yield of 78%; ^{1}H nmr: δ 0.72 (3H, d, J = 7 Hz), 0.95 (6H, m), 1.09 (3H, d, J = 7 Hz), 1.31 (3H, d, J = 7 Hz), 1.45-1.58 (1H, m), 1.84-1.98 (2H, m), 2.42-2.48 (1H, m), 2.59-2.79 (2H, m), 3.08 (1H, d-q, J = 10.4, 7 Hz), 4.11-4.21 (1H, m), 7.16-7.39 (10H, m).

Anal. Calcd. for $C_{28}H_{34}N_2O$: C, 81.12; H, 8.27; N, 6.76. Found: C, 81.13; H, 8.21; N, 6.29.

(2'*S*,3'*S*)-2-(2'-Methyl-3'-phenylpentanoyl)-3-phenyl-*l*-menthopyrazole (**7m**).

This compound was obtained in a yield of 63%; ^{1}H nmr: δ 0.60 (3H, d, J = 7 Hz), 0.74 (3H, t, J = 7 Hz), 0.93 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.15-1.29 (1H, m), 1.28 (3H, d, J = 7 Hz), 1.43-1.65 (2H, m), 1.83-1.95 (3H, m), 2.38-2.45 (1H, m), 2.61-2.66 (1H, m), 2.71-2.76 (1H, m), 2.86-2.93 (1H, m), 4.18-4.24 (1H, m), 6.70-6.72 (2H, m), 7.17-7.41 (8H, m).

Anal. Calcd. for $C_{29}H_{36}N_2O$: C, 81.27; H, 8.47; N, 6.54. Found: C, 81.22; H, 8.48; N, 6.24.

(2'*S*,3'*S*)-2-(2',4'-Dimethyl-3'-phenylpentanoyl)-3-phenyl-*l*-menthopyrazole (**7n**).

This compound was obtained in a yield of 16%; ^{1}H nmr: δ 0.58 (3H, d, J = 7 Hz), 0.79 (3H, d, J = 7 Hz), 0.87 (3H, d, J = 7 Hz), 0.93 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.12-1.29 (1H, m), 1.33 (3H, d, J = 7 Hz), 1.41-1.56 (1H, m), 1.74-2.03 (2H, m), 2.16-2.28 (1H, m), 2.37-2.49 (1H, m), 2.62-2.69 (1H, m), 2.73-2.81 (1H, m), 2.91-3.07 (1H, m), 4.44-4.56 (1H, m), 6.50 (2H, broad s), 7.03-7.53 (8H, m).

Anal. Calcd. for $C_{30}H_{38}N_2O$: C, 81.4; H, 8.65; N, 6.33. Found: C, 81.19; H, 8.60; N, 5.78.

(*S*)-Methoxycarbonylbenzyl (3*S*)-3-Methyl-3-phenylpropanoate from 6a and Methyl *S*-Mandelate.

The tetrahydrofuran (2 ml) solution of **6a** (0.49 mmole), methyl *S*-(+)-mandelate (0.54 mmole) and boron trifluoride etherate (3.57 mmole) was refluxed for 10 hours under nitrogen atmosphere. The mixture was poured into water, extracted with dichloromethane and dried over anhydrous magnesium sulfate. The diastereomer ratio was evaluated from the nmr intensity of the peaks at δ 5.87 and 5.90 ppm. ^{1}H nmr: δ 0.77 (3H, d, J = 6.6 Hz), 3.65 (3H, s), 5.87 (0.17H, s), 5.90 (0.83H, s), 7.12-7.51 (10H, m).

Hydrolysis of Conjugate Adduct (**7**).

To a methanol (50 ml) solution of a conjugate adduct **7** (2.1 mmole) was added 2*N* aqueous sodium hydroxide (25 ml), and the mixture was stirred for 1.5 hours at room temperature. The mixture was diluted with water, washed with ether, and then acidified with dilute hydrochloric acid. The acidic product was extracted with dichloromethane and the organic layer was dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was recrystallized from hexane, and the product was identified with authentic data [14].

3*S*-3-Phenylbutanoic Acid.

This compound was obtained in a yield of 44%; $[\alpha]_D$: +37.9° (c 2.92, benzene); ^{1}H nmr: δ 1.29 (3H, d, J = 6.9 Hz), 2.59 (2H, d-AB-q, J = 15.5, 6.5 Hz), 3.18-3.32 (1H, m), 7.16-7.30 (5H, m), 10.97 (1H, broad s).

(2*S*,3*S*)-2-(2-Methyl-3-phenyl)butanoic Acid [18].

This compound was obtained in a yield of 44%; ^{1}H nmr: δ 0.99 (3H, d, J = 6.9 Hz), 1.33 (3H, d, J = 6.9 Hz), 2.62 (1H, d-q, J = 9.9, 6.9 Hz), 2.93 (1H, d-q, J = 9.9, 6.9 Hz), 7.17-7.34 (5H, m).

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