Notes

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A Synthesis of Simple 4,4-Disubstituted Tetrahydroisoquinolines by Cyclization of α,α-Disubstituted Phenylacetamides

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Cyclization of *N*-methyl-3,4-dimethoxyphenylacetamide (**1**) with paraformaldehyde in formic acid afforded 6,7-dimethoxy-3-isochromanone (**2b**). In contrast, the same reaction of α,α-disubstituted phenylacetamides (**5a**, **b**, **d**) gave the corresponding 4,4-disubstituted isoquinolin-3-ones (**7a**—**c**). However, the α-allylphenylacetamide (**5c**) gave the azepinone (**8**) as the main product. On the other hand, the carbamate (**6e**) afforded the 4-allylisoquinoline (**10**).

Keywords——4,4-disubstituted isoquinoline; isoquinolin-3-one; isoquinoline cyclization; *N*-acyliminium ion; azepine; *N*-acyliminium ion cyclization

Many methods are available for the preparation of simple tetrahydroisoquinolines.[1,2] Since many simple tetrahydroisoquinolines show pharmacological activities and some of them may be useful clinically,[1] development of new synthetic methods yielding simple tetrahydroisoquinolines should still be of interest. During an investigation of a new synthesis of simple 4,4-disubstituted tetrahydroisoquinolines by using phenylacetamides as starting materials, we examined the reactivity of 3,4-dioxygenated phenylacetamides from the view point of possible formation of *N*-acyliminium ion intermediates leading to isoquinolin-3-ones. Although the reaction of the phenylacetamide (**1**) with benzaldehyde in trifluoroacetic acid gave the 1-phenylisoquinolin-3-one (**2a**),[3] no general work has been done on the synthesis of 6,7-dioxygenated tetrahydroisoquinolin-3-ones by direct ring closure with a one-carbon unit such as formaldehyde or its equivalents. Indeed, cyclization of **1** with paraformaldehyde in formic acid (HCOOH) gave a quantitative yield of isochromanone (**2b**)[4] without formation of **2c**. We examined the same reaction with α,α-disubstituted 3,4-dimethoxyphenylacetamides based on the assumption that the tendency to form the *N*-acyliminium ion might be increased by the introduction of substituted at the α-position of **1**, and a preference for the formation of isoquinolin-3-ones was observed. The results of our studies are described in this paper.

The amides used for this study were prepared as follows. Ethyl diarylacetates were obtained by an application of Tamura's method.[5] Chlorination of ethyl α-methylthiophenylacetate (**3a**)[5] with *N*-chlorosuccinimide, followed by condensation with veratrole in the presence of stanic chloride afforded the ester (**4a**). Desulfurization of **4a** with zinc in acetic acid gave the ester (**4b**), methylation of which (lithium diisopropylamide, **4b**, methyl iodide, tetrahydrofuran, −78 °C) yielded the ester (**4c**). Hydrolysis of **4c** with 10% ethanolic sodium hydroxide gave the acid (**4d**). The reaction of the α-chlorinated ester (obtained by chlorination of ethyl α-methylthiopropionate (**3b**)[6] with *N*-chlorosuccinimide) with veratrole afforded the ester (**4e**), which was converted to the acid (**4f**) by hydrolysis. The allylation of the ester (**4g**),[7] followed by hydrolysis of the methyl allylacetate (**4h**) gave the acid (**4i**). The acids (**4d**, **4f**, and **4i**) thus obtained, and α,α-dimethyl-3,4-dimethoxyphenylacetic acid (**4j**),[8] were led to the

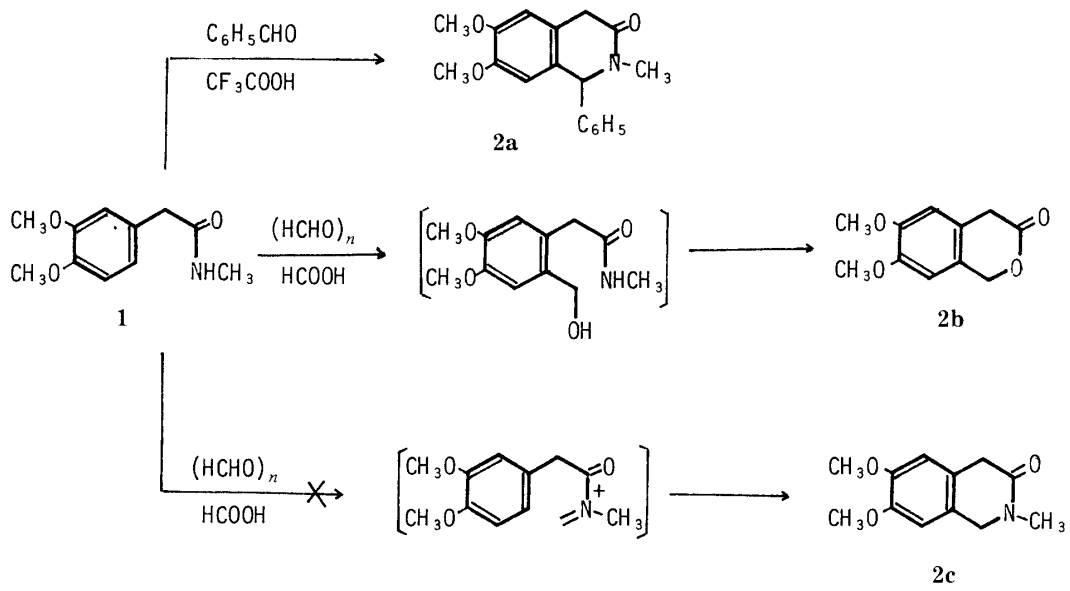

Chart 1

corresponding *N*-methylamides (**5a**—**d**) in the usual way.

Furthermore, the carbamate (**6e**) was prepared by ethoxycarbonylation of the amine (**6d**) derived from the ester (**6a**) through the procedure (**6a**→**6b**→**6c**→**6d**) involving phthalimidation of the alcohol (**6b**) by an application of Mitsunobu's method.[9] The compounds (**5a**—**d** and **6e**) were subjected to the cyclization reaction with paraformaldehyde in HCOOH. Treatment of **5a** with paraformaldehyde in HCOOH at 60—70 °C for 6 h afforded the 4-methyl-4-phenylisoquinolin-3-one (**7a**) without formation of the corresponding isochromanone. In a similar way, **5b** and **5d** were converted to the 4,4-disubstituted isoquinolin-3-ones (**7b** and **7c**, respectively). However, in the case of **5c**, cyclization proceeded mainly at the olefinic carbon to yield the azepinone (**8**) accompanied with the formation of a trace amount of 4-allylisoquinolin-3-one (**9**).[10] In this case, the formation of **8** seems to be either kinetically or thermodynamically more favorable than that of **9** owing to the dipole repulsion between the olefinic double bond and benzene ring (or carboxyl of the amide). It is interesting that the same cyclization reaction with **6e** gave exclusively the isoquinoline (**10**). Reduction of **7a** with lithium aluminum hydride gave the 2,4-dimethyl-4-phenyltetrahydroisoquinoline (**11**) in nearly quantitative yield. Thus, ring closure of α,α-disubstituted 3,4-dioxygenated phenylacetamides with paraformaldehyde in HCOOH was found to be useful for the synthesis of 4,4-disubstituted tetrahydroisoquinolines.

Experimental[11]

6,7-Dimethoxy-3-isochromanone (2b)——A mixture of **1** (2.09 g, 10 mmol), paraformaldehyde (0.6 g, 20 mmol) and HCOOH (15 ml) was stirred at room temperature for 14 h.[12] The mixture was made basic with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated to give **2b** (1.77 g, 92%), mp 108—109 °C, which gave physical data identical with those recorded in the literature.[4]

Ethyl α-Methylthio-α-phenyl-3,4-dimethoxyphenylacetate (4a)——*N*-Chlorosuccinimide (4.82 g, 36 mmol) was added in small portions to a stirred solution of **3a** (6.3 g, 30 mmol) in CCl_4 (100 ml) at 0 °C. After stirring had been continued for 1.5 h at the same temperature, succinimide was filtered off and the filtrate was evaporated. $SnCl_4$ (7.76 g, 30 mmol) was added to a mixture of the remaining residue, veratrole (6.21 g, 45 mmol) and CH_2Cl_2 (40 ml) under stirring at 0 °C. After stirring had been continued for 1 h, the mixture was diluted with H_2O and extracted with $CHCl_3$. The extract was washed with 5% aq. NaOH and H_2O, then dried (Na_2SO_4), and evaporated. The resulting residue was chromatographed on silica gel (30 g). Elution with AcOEt–hexane (1 : 5, v/v) gave **4a** (3.37 g, 76%), mp 68.5—69 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.22 (3H, t, J=7 Hz, CH_3CH_2O), 1.91 (3H, s, CH_3S), 3.81, 3.89 (6H, each s, 2×CH_3O), 4.28 (3H, q, J=7 Hz, CH_3CH_2O), 6.77—7.17 (3H, m, Ar-H), 7.27—7.56 (5H, m, Ar-H). Mass spectrum

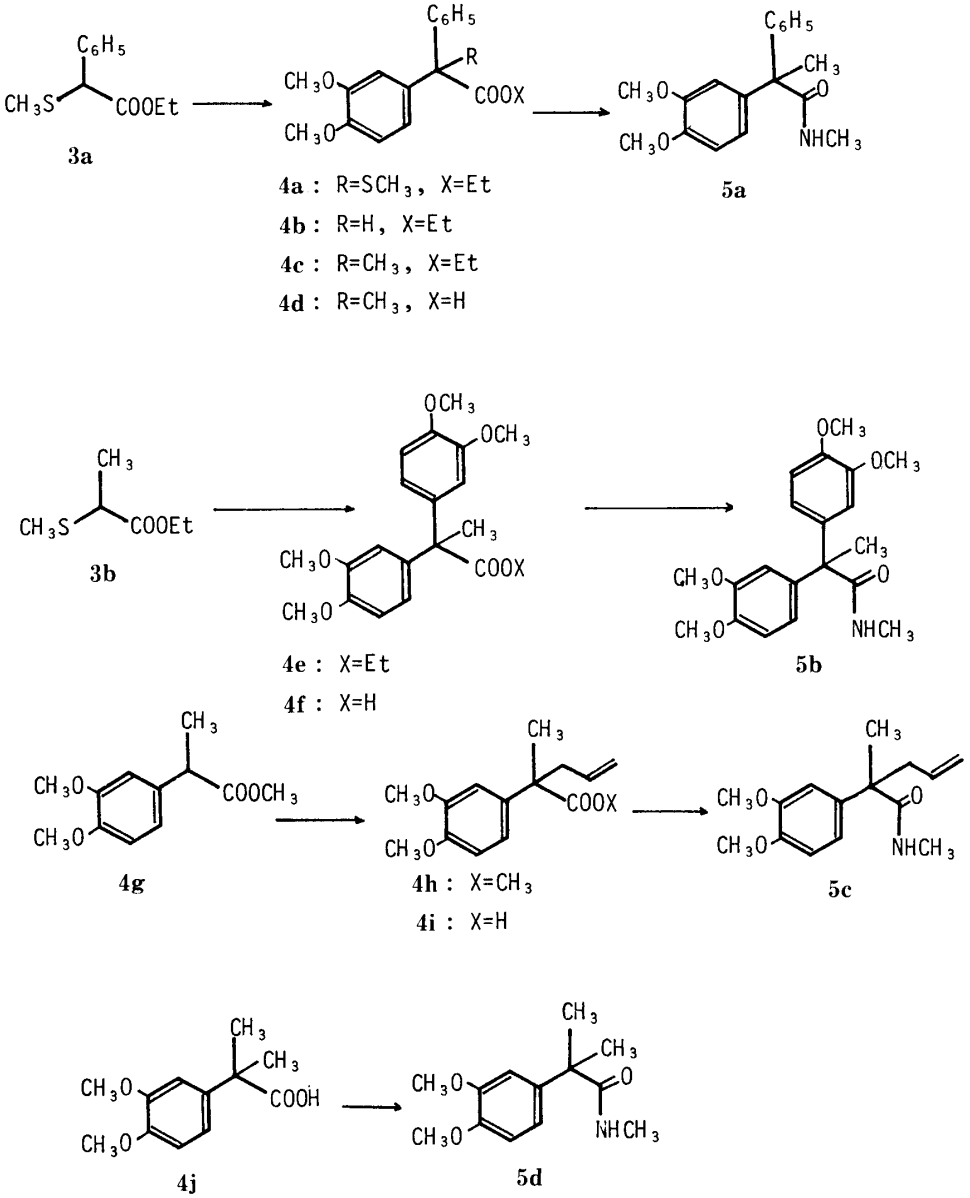

Chart 2

(MS) *m/e*: 346 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (ester). *Anal.* Calcd for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40. Found: C, 65.87; H, 6.36.

Ethyl α-Phenyl-3,4-dimethoxyphenylacetate (4b)——A mixture of **4a** (1.1 g, 3 mmol), Zn (2.70 g, 6 mmol) and AcOH (60 ml) was heated under stirring at 110 °C for 1 h. After cooling, the mixture was diluted with H_2O (200 ml) and extracted with benzene. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated to leave **4b** (0.78 g, 87%) as an oil; this was used for the following reaction without purification. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (3H, t, J= 7 Hz, CH_3CH_2O), 3.86, 3.88 (6H, each s, 2 × CH_3O), 4.24 (2H, q, J=7 Hz, CH_3CH_2O), 5.00 (1H, s, ArCH), 6.90—7.00 (3H, m, Ar-H), 6.91—7.48 (5H, m, Ar-H).

2-(3,4-Dimethoxyphenyl)-2-phenylpropionic Acid (4d)——A solution of **4b**. (12 g, 40 mmol) in tetrahydrofuran (THF) (20 ml) was added to a solution of lithium diisopropylamide (LDA) (44 mmol, prepared from 4.4 g of diisopropylamine and 26 ml of 1.65 M hexane solution of *n*-BuLi) in THF (40 ml) under stirring at −78 °C. After 0.5 h, CH_3I (6.25 g, 44 mmol) was added to this solution. After stirring had been continued for 1 h, the mixture was poured into H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated. A solution of the remaining residue (**4c**) in 10% EtOH–NaOH (200 ml) was refluxed for 2 h. The solvent was evaporated off and the resulting residue was made acidic with 10% HCl and extracted with $CHCl_3$. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated to give **4d** (9.84 g, 86%), mp 127—128 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.93 (3H, s, CH_3), 3.77, 3.88 (6H, each s, 2 × CH_3O), 6.88 (3H, br s, Ar-H), 7.33 (5H, br s, Ar-H). MS *m/e*: 286 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (COOH). *Anal.* Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.19; H, 6.35.

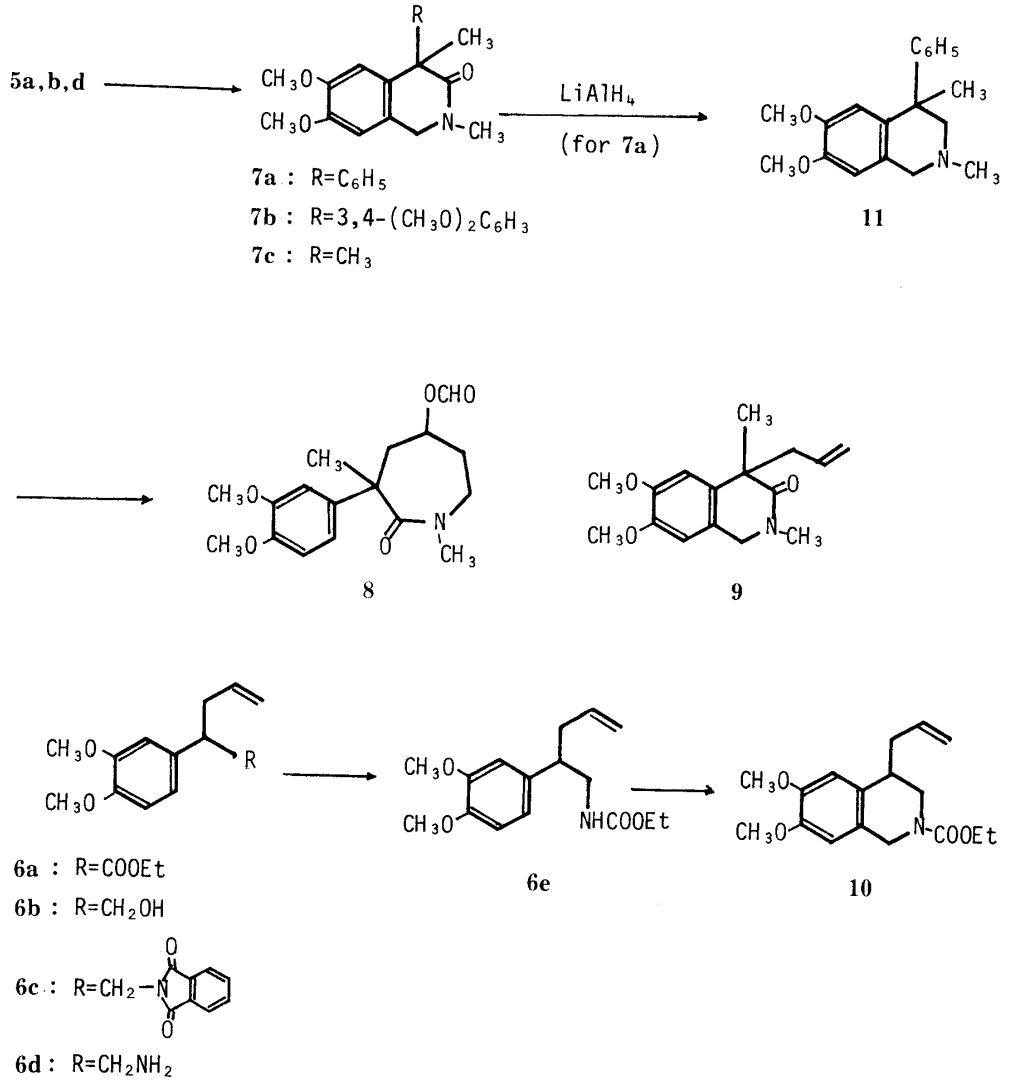

Chart 3

2,2-Di-(3,4-dimethoxyphenyl)propionic Acid (4f)——*N*-Chlorosuccinimide (4.92 g, 36 mmol) was added to a stirred solution of **3b** (4.44 g, 30 mmol) in CCl_4 (100 ml) and worked up as above. $SnCl_4$ (7.76 g, 30 mmol) was added to a mixture of the resulting residue, veratrole (12.4 g, 90 mmol) and CH_2Cl_2 (40 ml) under stirring at 0°C. After stirring had been continued for 2 h at the same temperature, the mixture was diluted with H_2O and extracted with $CHCl_3$. The extract was washed with 5% aq. NaOH and H_2O, then dried (Na_2SO_4), and evaporated. The resulting residue was chromatographed on silica gel (30 g) with AcOEt–hexane (1 : 3, v/v) as an eluent. The first fraction (60 ml) was discarded, and evaporation of the second one (150 ml) gave **4e** (6.03 g, 53.8%) as an oil. A solution of this oil in 10% EtOH–NaOH (200 ml) was refluxed for 2 h and worked up as above to give **4f** (4.91 g, 88%), mp 154—155 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.93 (3H, s, $C\underline{H}_3$), 3.79, 3.91 (each 6H, each s, $4 \times C\underline{H}_3O$), 6.90 (6H, s, Ar-$\underline{H}$). MS *m/e*: 346 ($M^+$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (COOH). *Anal.* Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.65; H, 6.46.

2-(3,4-Dimethoxyphenyl)-2-methyl-4-pentenoic Acid (4i)——A solution of **4g** (8.96 g, 40 mmol) in THF (20 ml) was added to a solution of LDA (44 mmol, prepared as above) in THF (40 ml) under stirring at −78 °C. After 0.5 h, allyl bromide (5.32 g, 44 mmol) was added to this solution and the mixture was worked up as usual. The resulting ester was hydrolyzed and worked up as in the preparation of **4d** to give **4i** (8.30 g, 83%) as an oil. ^{1}H-NMR ($CDCl_3$) δ: 1.56 (3H, s, $C\underline{H}_3$), 2.57—2.98 (2H, m, $C\underline{H}_2$–CH=CH_2), 3.87 (6H, s, $2 \times C\underline{H}_3O$), 4.50—5.24 (2H, m, $C\underline{H}_2$=CH), 5.43—5.98 (1H, m, CH_2=C$\underline{H}$), 6.78—7.08 (3H, m, Ar-$\underline{H}$). MS *m/e*: 250 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (COOH), 1640 (C=C).

General Procedure for the Synthesis of Amides (5a—d)——A mixture of the acid (10 mmol), $SOCl_2$ (1.78 g, 15 mmol) and dry benzene (40 ml) was heated under reflux for 2 h. $CH_3NH_2 \cdot HCl$ (1.35 g, 20 mmol) and Na_2CO_3 (4.24 g, 40 mmol) were added to this solution under stirring at 0—5 °C. After 5 min, H_2O (5 ml) was added, and the whole was stirred for 14 h at room temperature, then extracted with benzene. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated to give the product (**5a—d**). Yields, mps, IR spectral, and analytical data are summarized

Table I. Yields, mp, MS (*m/e*: M^+), IR Spectral, and Analytical Data for the Amides (**5a—d**)

Compound	Formula	Yield (%)	mp (°C)	MS (*m/e*: M^+)	IR cm^{-1} ($CHCl_3$)	Analysis (%) Calcd (Found)		
						C	H	N
5a	$C_{18}H_{21}NO_3$	80	133—134	299	3440 1670	72.21 (72.12	7.07 7.04	4.68 4.71)
5b	$C_{20}H_{25}NO_5$	78	128—129	359	3430 1665	66.83 (66.67	7.01 6.98	3.90 3.95)
5c	$C_{15}H_{21}NO_3$	82	87—88	263	3440 1660	68.41 (68.31	8.04 8.08	5.32 5.21)
5d	$C_{13}H_{19}NO_3$	88	65—66	237	3435 1665	65.80 (65.61	8.07 8.07	5.90 6.08)

in Table I.

Ethyl 2-(3,4-Dimethoxyphenyl)-4-pentenoate (6a)——A solution of ethyl 3,4-dimethoxyphenylacetate (8.96 g, 40 mmol) in THF (20 ml) was added to a solution of LDA (44 mol, prepared as above) in THF (40 ml) at −78 °C. After 0.5 h, allyl bromide (5.32 g, 44 mmol) was added to this solution. After stirring had been continued at the same temperature for 1 h, the mixture was poured into H_2O and extracted with benzene. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated to give **6a** (9.30 g, 88%), bp 150 °C (2 Torr). ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, t, J=7 Hz, $C\underline{H}_3CH_2O$), 2.33—3.00 (2H, m, $C\underline{H}_2CH=CH_2$), 3.60 (1H, t, J=6 Hz, ArC$\underline{H}$), 3.83, 3.87 (6H, each s, $2\times C\underline{H}_3O$), 4.17 (2H, q, J=7 Hz, $CH_3C\underline{H}_2O$), 4.99—5.20 (2H, m, $C\underline{H}_2=CH$), 5.57—6.03 (1H, m, $CH_2=C\underline{H}$), 6.83—6.97 (3H, m, Ar-$\underline{H}$). MS *m/e*: 264 (M^+). *Anal.* Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.36; H, 7.49.

2-(3,4-Dimethoxyphenyl)-4-penten-1-ol (6b)——A solution of **6a** (7.92 g, 30 mmol) in THF (50 ml) was added to a mixture of $LiAlH_4$ (2.22 g, 60 mmol) and THF (300 ml) under ice-cooling. After stirring had been continued for 14 h at room temperature, the mixture was worked up as usual to yield **6b** (6.13 g, 93%), bp 155 °C (2 Torr). ^{1}H-NMR ($CDCl_3$) δ: 2.33—2.97 (3H, m, C$\underline{H}$–$C\underline{H}_2CH=C$), 3.70 (2H, br d, J=5 Hz, $HOC\underline{H}_2$), 3.87, 3.89 (6H, each s, $2\times C\underline{H}_3O$), 4.97—5.13 (2H, m, $C\underline{H}_2=CH$), 5.77—6.00 (1H, m, $CH_2=C\underline{H}$), 6.73—6.93 (3H, m, Ar-$\underline{H}$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3570 (OH), 1640 (C=C). *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.04; H, 8.40.

***N*-[2-(3,4-Dimethoxyphenyl)-4-pentyl]-phthalimide (6c)**——Diisopropyl azodicarboxylate (5.05 g, 25 mmol) was added to a stirred solution of **6b** (5.55 g, 25 mmol), phthalimide (3.68 g, 25 mmol), and triphenylphosphine (6.55 g, 25 mmol) in THF (35 ml) under ice-cooling. After stirring had been continued for 14 h at room temperature, the solvent was evaporated off and the remaining residue was chromatographed on silica gel (40 g). Elution with benzene–hexane (1 : 1, v/v) gave **6c** (6.84 g, 78%), mp 97—98 C. MS *m/e*: 351 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775, 1706 (C=O), 1640 (C=C). *Anal.* Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.55; H, 6.24; N, 4.20.

Ethyl-*N*-[2-(3,4-Dimethoxyphenyl)-4-pentenyl]carbamate (6e)——A mixture of **6c** (6 g, 17.1 mmol), hydrazine hydrate (4 ml of 80% solution) and EtOH (40 ml) was heated for 14 h under reflux. The solvent was evaporated off and the remaining residue was suspended in 5% HCl (40 ml); insoluble material was removed by filtration. The filtrate was made basic with K_2CO_3 and extracted with benzene. The extract was dried (Na_2SO_4) and evaporated to give **6d** as an oil, which was used for the following reaction without purification. ClCOOEt (2.7 g, 25 mmol) was added to a mixture of **6d**, Et_3N (5.05 g, 50 mmol) and benzene (70 ml) under ice-cooling. After stirring had been continued for 3 h, the mixture was washed with 5% HCl and H_2O, then dried (Na_2SO_4), and evaporated to leave **6e** (5.7 g, 78%) as an oil. MS *m/e*: 293 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, t, J=7 Hz, $C\underline{H}_3CH_2O$), 2.27—3.53 (5H, m, $NC\underline{H}_2C\underline{H}$–$C\underline{H}_2C=C$), 2.37 (6H, s, $2\times C\underline{H}_3O$), 4.15 (2H, q, J=7 Hz, $CH_3C\underline{H}_2O$), 4.09—5.09 (2H, m, $C\underline{H}_2=CH$), 5.48—5.87 (1H, m, $CH_2=C\underline{H}$), 6.63—6.83 (3H, m, Ar-H). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440 (NH), 1705 (C=O), 1640 (C=C).

Reaction of 5a—d and 6e with Paraformaldehyde in HCOOH——A mixture of **5** (or **6e**) (10 mmol), paraformaldehyde (0.6 g, 20 mmol) and HCOOH (15 ml) was stirred at 60—70 °C for 6 h. The mixture was made basic with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with H_2O, dried (Na_2SO_4), and evaporated. The products (**7a—c**) were obtained by recrystallization of the resulting solid from methanol–ether. The products (**8** and **10**) were obtained by column chromatography on silica gel (20 g) with AcOEt–hexane (1 : 1, v/v) as the eluent, with monitoring by TLC. Yields and physical data are summarized in Table II.

1,2,3,4-Tetrahydro-6,7-dimethoxy-2,4-dimethyl-4-phenylisoquinoline (11)——A solution of **7a** (1.25 g, 4 mmol) in THF (20 ml) was added to a solution of $LiAlH_4$ (0.5 g, 13.5 mmol) in THF (50 ml) under stirring. After stirring had been continued at room temperature for 14 h, the mixture was worked up as usual to give **11** (1.11 g, 93%), mp 96—98 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.73 (3H, s, $C\underline{H}_3$), 2.33 (3H, s, $NC\underline{H}_3$), 2.61 (2H, s, 3-$\underline{H}_2$), 3.57 (2H, s, 1-$\underline{H}_2$), 3.67, 3.87 (6H, each, s, $2\times C\underline{H}_3O$), 6.39 (1H, s, 5-$\underline{H}$), 6.57 (1H, s, 8-$\underline{H}$), 7.27 (5H, br s, 4-Ar-$\underline{H}$). MS *m/e*: 297 ($M^+$). *Anal.* Calcd

TABLE II. Yields and Physical Data for **7a**—**c**, **8** and **10**

Compound	Formula	Yield (%)	mp (°C)	MS (*m/e*: M^+)	IR cm^{-1} ($CHCl_3$)	^{1}H-NMR ($CDCl_3$) δ	Analysis (%) Calcd (Found)		
							C	H	N
7a	$C_{19}H_{21}NO_3$	74	109—110	311	1640	1.92 (3H, s, 4-CH_3), 3.08 (3H, s, NCH_3), 3.90, 3.93 (6H, each s, 2×CH_3O), 4.09 (1H, d, J=16 Hz, 1-H), 4.20 (1H, d, J=16 Hz, 1-H), 6.76 (1H, s, 5-H), 6.92 (1H, s, 8-H), 7.03—7.43 (5H, m, Ar-H)	73.08 (73.29	6.75 6.84	4.47 4.50)
7b	$C_{21}H_{25}NO_5$	82	174—176	371	1655	1.85 (3H, s, 4-CH_3), 3.02 (3H, s, NCH_3), 3.72, 3.75, 3.82, 3.85 (each 3H, each s, 4×CH_3), 4.03 (1H, d, J= 18 Hz, 1-H), 4.18 (1H, d, J=16 Hz, 1-H), 6.36—6.52 (1H, m, Ar-H), 6.64—7.69 (2H, m, Ar-H), 6.70 (1H, s, 5-H), 6.84 (1H, s, 8-H)	67.60 (67.90	6.70 6.78	3.55 3.77)
7c	$C_{14}H_{19}NO_3$	80	103—104	249	1660	1.61 (6H, s, 4-CH_3), 3.10 (3H, s, NCH_3), 3.80, 3.90 (6H, each s, 2×CH_3O), 4.46 (2H, s, 1-H), 6.66 (1H, s, 5-H), 6.87 (1H, s, 8-H)	67.33 (67.44	7.65 7.68	5.58 5.67)
8	$C_{17}H_{23}NO_5$	78	109—110	321	1720	1.45 (3H, s, 3-CH_3), 3.14 (3H, s, NCH_3), 3.90, 3.96 (6H, each s, 2×CH_3O), 5.22—5.59 (1H, m, C<u>H</u>OCHO), 6.74—7.00 (3H, m, Ar-H), 8.14 (1H, s, CHOC<u>H</u>O)	63.56 (63.53	7.23 7.21	4.30 4.36)
10	$C_{17}H_{23}NO_4$	84	Oil	305	1690 1640	1.33 (3H, t, J=7 Hz, C<u>H</u>$_3$$CH_2O$), 2.25—2.42 (2H, m, CH_2C=), 2.78—4.12 (3H, m, 3-H, 4-H), 3.90 (6H, s, 2×CH_3O), 4.23 (2H, q, J=7 Hz, CH_3C<u>H</u>$_2$O), 4.33 (1H, d, J=17 Hz, 1-H), 4.83 (1H, d, J=17 Hz, 1-H), 5.07—5.23 (2H, m, CH_2=), 5.73—6.20 (1H, m, CH_2=C<u>H</u>), 6.67 (1H, s, 5-H), 6.76 (1H, s, 8-H)			

for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.59; H, 7.82; N, 4.60.

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9) O. Mitsunobu, M. Wada, and T. Sano, *J. Am. Chem. Soc.*, **94**, 679 (1972).
10) Although the ^{1}H-NMR ($CDCl_3$) spectrum of the crude product indicated the presence of **9**, it was difficult to isolate this compound in the pure state.
11) Melting points were taken on a Yanagimoto micro melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a Varian EM-390 instrument. Mass spectral data were obtained at an ionizing voltage of 70 eV on a Hitachi RMU-7L instrument. Infrared (IR) spectra were taken on a JASCO IRA-1 spectrometer. THF was distilled from $LiAlH_4$ before use. HCOOH used in this study was of the best commercial grade available. All reactions were carried out under N_2 unless otherwise noted.
12) Although the reaction was examined at 60—70 C as in the synthesis of **7a—c**, **2b** was obtained as the sole product in 90% yield.