Pharmacological Activities of the Prenyl coumarins, Developed from Folk Usage as a Medicine of *Peucedanum japonicum* THUNB. 1\(^{1}\)

Naoki Takeuchi,\(^{a}\) Toshio Kasama,\(^{a}\) Yoko Aida,\(^{a}\) Junji Oki,\(^{a}\) Izumi Maruyama,\(^{a}\) Kiyoshi Watanabe,\(^{b}\) and Seisho Tobinaga\(^{a}\;\( ^{a}\)\)

Showa College of Pharmaceutical Sciences,\(^{a}\) Machida, Tokyo 194, Japan and Research laboratory of Biological Sciences, Kodama Ltd.,\(^{a}\) Matsudo, Chiba 271, Japan. Received October 8, 1990

In connection with the chemical structure of coumarin 1 (a mixture of acetylangeloylkhellactone and acetyl-tigloylkhellactone), a compound isolated from *Peucedanum japonicum* THUNB., we synthesized eight coumarin compounds (3–10) and performed pharmacological studies on these nine compounds, as well as on another coumarin, praeuprtorin A (=Pd-Ia) (2), a compound isolated from *Peucedanum praeruptorium* DUNN. We studied the effects of compounds 1–5 on isolated smooth muscle and of compounds 1–10 on the cardiovascular system. These compounds showed dose-related antagonistic effects on histamine- and Ca\(^{2+}\)-induced contractions in smooth muscle and the potencies were in the order 2 > 1 > seselin (3) > xanthyletin (4) = 2,2,10-trimethyl-2H,8H-benz[1,2-b; 3,4-b']dipyran-9-one (5). All the compounds except 7-geranyloxy-4-methylcoumarin (10) produced a dose-related increase in vertebrocarotid and femoral blood flow. Compounds 1, 5, and 4-methyl-7-(3-methyl-2-butenyloxy)coumarin (8) caused an increase in blood pressure, but 3 and 4 caused a slight decrease. Compounds 2, 3, 4, 5, and 8 increased heart rate. Jatamansine (6) and jatamansinol (7) caused only small changes in blood pressure. All the compounds except 10 increased heart rate. Compound 1 also increased blood flow in the cerebral cortex. Thus, compound 1 was confirmed to have an inhibitory effect on contraction in isolated smooth muscle and an action increasing arterial blood flow. Among the compounds tested in this study, 3, as well as 6 and 7 synthesized on the basis of 3, showed actions similar to those of Ca\(^{2+}\) blockers and some compounds had papaverine-like activities. These results suggest that the chemical moiety of compound 3 may be the basis for the pharmacological activities of *Peucedanum japonicum* THUNB.

Keywords *Peucedanum japonicum*; *Peucedanum praeruptorium*; coumarin; seselin; synthesis; smooth muscle contraction; arterial blood flow; calcium ion blocker

The leaves and roots of *Peucedanum japonicum* THUNB. have been used as a wholesome vegetable (folk name: chyomeigusa) and a folk medicine for the treatment of coughs, respectively, in the Ryukyu Islands.\(^{2}\) The plant, called chyomeigusa (grass for longevity), is indispensable in dishes served in ceremonies such as shirayoi (ceremony for naming a newborn) and yahnuoyi (celebration of the completion of a new house) in the Yaeyama Islands.\(^{3}\) Coumarin 1 (a mixture of acetylangeloylkhellactone and acetyl-tigloylkhellactone) is reported to be one of the principal constituents of this plant.\(^{4}\) On the other hand, there is a plant called zenko (*Peucedanum praeruptorium* DUNN.) a relative of chyomeigusa, among Chinese medicines. It is reported that zenko contains coumarins which have concompetitive anticholinergic, antihistaminic, and Ca\(^{2+}\) blocking actions and that praeruptorin A (Pd-Ia; 2) is the most active compound among them.\(^{5}\)

We are interested in the relationship between the folk usage of chyomeigusa as a medicine and the pharmacological activities of coumarin 2, and compared the pharmacological

![Chart 1](https://example.com/chart1.png)

© 1991 Pharmaceutical Society of Japan
activities of coumarin 1 with those of coumarin 2. Further, in order to investigate the structural requirement for the activities of the two compounds, we synthesized eight related compounds, seselin (3), xanthyletin (4), 2,2,10-trimethyl-2H,5H-benzo[1,2-b:3,4-b']dipyran-8-one (5), jatamansinone (6), jatamansinol (7), 4-methyl-7-(3-methyl-2-butenyloxy)coumarin (8), 7-(2-dimethylaminoethoxy)-4-methylcoumarin hydrochloride (9), and 7-geranyl氧-4-methylcoumarin (10) and examined their pharmacological activities. We performed the following pharmacological studies: (1) experiments with isolated smooth muscle; histamine- and Ca^{2+}-induced contraction in guinea pig ileum and (2) experiments with the car diovascular system; blood flow, blood pressure, and heart rate in dogs and cerebral blood flow in rabbits.

**Materials** Coumarins 1 and 2 were isolated from the ether extracts of the roots of *Peucedanum japonicum* THUNB. and the methanol extracts of the roots of *Peucedanum praeruptorum* DUNN. Seselin (3) and xanthyletin (4) were synthesized from umbelliferone. Coumarin 5 was synthesized from 2,6-dihydroxyacetophenone as shown in Chart 2. That is, the reaction of 2,6-dihydroxyacetophenone with diethyl malonate in the presence of tetrabutylammonium fluoride gave the condensation product 11 (82.1% yield) which was transformed to the acid 12 by hydrolysis with 10% KOH in 88.8% yield. The resulting acid was converted to 13 by decarboxylation at 240°C in 90.7% yield. Coumarin 13 and 3-chloro-3-methylbutyne were condensed in the presence of NaH in 

\[ N,N\text{-dimethylformamide (DMF)} \] to give the product 14 in 35.6% yield. The conversion of 14 to 5 was established by heating with 

\[ N,N\text{-dimethylformamide (DMF)} \] in 82.0% yield. Jatamansinone (6) and jatamansinol (7) were synthesized from seselin (3) by the method of Bohlman and Hata. Coumarins 8, 9, and 10 were synthesized by the reactions of 8-hydroxy-4-methylcoumarin with 4-bromomethyl-2-butenone, 2-chloroethylmethylammonium chloride, and geranyl chloride in the presence of K_2CO_3 in DMF in yields of 61.0, 21.0, and 89.0%, respectively.

**Agents** Coumarins 1, 2, 3, 4, 5, 6, 7, 8, and 10 were dissolved in ethanol and diluted with water or saline for *in vitro* or *in vivo* studies and suspended in 0.5% (w/v) carboxymethyl cellulose (CMC) for *in vivo* study. Compound 9 was dissolved in water. Other agents used were histamine dihydrochloride (histamine; Wako Pure Chemical Industries, Ltd.), CaCl_2 (Ca^{2+}; Wako Pure Chemical Industries, Ltd.), KCl (K^{+}; Wako Pure Chemical Industries, Ltd.), diphenylhydramine hydrochloride (diphenhydramine; Wako Pure Chemical Industries, Ltd.), sodium pentobarbital (Tokyo Kasei Co., Ltd.), \(d\)-tubocurarine chloride (Wako Pure Chemical Industries, Ltd.), and diltiazem (Tanabe Seiyaku Co., Ltd.; extracted from the tablets in our laboratory).

**Animals** Male Hartley strain guinea pigs weighing about 200 g (Japan SLC, Inc.), male albino rabbits weighing about 2.5 kg (Japan Laboratory Animal Inc.), and adult mongrel dogs weighing 9.0 to 16 kg (Takeda Kaseijyo Co., Ltd.) were acclimatized for more than one week after purchase. The animals that had been in good health during the acclimatization period were selected for use in this study. They were housed in rooms controlled to maintain temperature and relative humidity at 22 ± 3°C and 55 ± 10%, respectively, with air change 10 to 15 times/h and 12 h (07:00—19:00) of artificial light.

**Methods** (1) Experiments with Isolated Smooth Muscle (i) Effects of Coumarins on Histamine-Induced Contraction
in Isolated Guinea Pig Ileum: The guinea pigs were sacrificed by a sharp blow to the head and the ileum removed. The preparation was suspended in a 10 ml organ bath of Tyrode's solution maintained at 26°C and bubbled with 95% O₂ and 5% CO₂. Contractile responses were measured with an isotonic transducer (ME-4012, Medical Electrics Co. and TD1125—DT1125, Nihon Kodens Corporation) and the resting tension was set at 0.5 g. Compounds were applied at 5 min before the addition of the agonist.

(ii) Effects of Coumarins on Ca²⁺-Induced Contraction in Isolated Guinea Pig Ileum: The preparation suspended as described in (i) was washed with Ca-free Locke-Ringer's solution added with 1 mM ethylenediaminetetraacetic acid (EDTA) for 40 to 60 min. Then, the preparation was placed in Ca-free Locke-Ringer's solution. After an addition of 75 mM K⁺ (final concentration; 80 mM K⁺) to the solution, Ca²⁺ was cumulatively added to induce contraction of the ileum. Compounds were applied at 5 min before the addition of 75 mM K⁺.

(2) Experiments with Cardiovascular System Adult mongrel dogs were anesthetized with sodium pentobarbital (30 mg/kg, i.v.). The trachea was cannulated for artificial respiration (Harberd). Blood pressure in the left femoral artery and heart rate were routinely measured by means of a pressure transducer (MPU-0.5, Nihon Kodens Corporation) and a cardiograph (AT-601G, Nihon Kodens Corporation), respectively. Mean blood flow was measured with an electromagnetic flow meter (FM-27, Nihon Kodens Corporation) in three blood vessels: right carotid, right vertebral, and right femoral arteries. Compounds were given in the cannulated left femoral vein.

(3) Statistical Method Student's t-test was used for statistical analysis.

Results and Discussion

(1) Effects of Coumarins on Isolated Smooth Muscle (i) Effects of Coumarins on Histamine-Induced Contraction:

Compounds 2 at 10⁻⁶ g/ml or more, 1, 3, and 5 at 10⁻⁵ g/ml or more, and 4 at 3 x 10⁻⁵ g/ml or more caused a rightward shift of the dose–response curve for histamine with a reduction of the maximal responses (Fig. 1). The vehicle (ethanol: 0.01—0.5% (v/v)) showed no effect on the histamine-induced contraction. Table I summarized the pD₂ values of drugs and the antagonistic potencies were in the order 2 > 1 > 3 > 5 > 4. Diphenhydramine, a histamine antagonist, caused a parallel shift of the dose–response curve without a reduction of the maximal response.

(ii) Effects of Coumarins on Ca²⁺-Induced Contraction: Compounds 1 and 2 at 10⁻⁶ g/ml and 3 at 3 x 10⁻⁶ g/ml produced a slight shift of the dose–response curve for Ca²⁺ to the right (Fig. 2). However, 1 and 2 at 3 x 10⁻⁶ g/ml or more and 3 at 10⁻⁵ g/ml or more further shifted the curves to the right with the concomitant decrease in the maximum responses. Compounds 4 and 5 at 10⁻⁵ or more and 3 x 10⁻⁴ g/ml or more, respectively, showed a noncompetitive antagonistic tendency of the Ca²⁺-induced contraction. The vehicle showed no effect on this contraction. Table I summarized the pD₂ values of drugs and the Ca²⁺-antagonistic potencies were in the order 2 > 1 > 3 > 4 > 5.

Table I. Antagonistic Activity of Drugs on Histamine- and Ca²⁺-Induced Contraction in the Isolated Guinea Pig Ileum

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Antagonistic activity (pD₂; mean ± S.E.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>6</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>—</td>
</tr>
</tbody>
</table>

Table continues...

Fig. 1. Effects of 1, 2, 3, 4, 5 and Diphenhydramine (Dip.) on Histamine-Induced Contraction in the Isolated Guinea Pig Ileum

--- control; ——— 10⁻⁶; ——— 10⁻⁷; ——— 10⁻⁸; ——— 10⁻⁹; ——— 10⁻¹⁰; ——— 3 x 10⁻⁵; ——— 10⁻⁴ g/ml. Each point represents the mean ± S.E. of 5 to 6 experiments.
Fig. 2. Effects of 1, 2, 3, 4, 5 and Diltiazem (Dil.) on Ca^{2+}-Induced Contraction in the Isolated Guinea Pig Ileum

---, control; ---, 10^{-6}; ----, 10^{-6}; ---, 10^{-4}; ---, 3 \times 10^{-4}; ----, 10^{-5}; ----, 3 \times 10^{-5}; ---, 10^{-8} g/ml. Each point represents the mean ± S.E. of 5 to 6 experiments.

Fig. 3. Effects of Coumarins (1—10) and Other Drugs on Carotid, Vertebral and Femoral Arterial Blood Flows in Anesthetized Dogs

D, diltiazem; P, papaverine; ---, carotid; ----, vertebral; ---, femoral artery. Each point represents the mean ± S.E. of 5 to 7 experiments.
Diltiazem, a Ca\(^{2+}\) blocker, caused a parallel shift of the dose–response curve.

(2) Effects of Coumarins on Cardiovascular System

Since compounds 1–5 showed inhibitory effects on histamine- and Ca\(^{2+}\)-induced contractions, compounds 6–10 in addition to 1–5 were studied for their effects on blood flow, blood pressure, and heart rate. As values (mean ± S.E.) before treatment with the test compounds, blood flow was 34.4 ± 1.4 ml/min for vertebral artery, 140.0 ± 3.9 ml/min for carotid artery and 60.4 ± 2.2 ml/min for femoral artery, and systolic blood pressure was 193.0 ± 1.3 mmHg, diastolic blood pressure was 125.3 ± 1.2 mmHg and heart rate was 168.4 ± 1.7 beat/min. All the compounds except 10 produced dose-related effects on these cardiovascular parameters (Figs. 3–5). Compounds 1–9 increased blood flow. The percent increase in carotid and vertebral blood flow was larger than that in femoral blood flow at 1.0 mg/kg or more of 1. Compounds 2 and 3 at 0.3 mg/kg or more and at 1.0 mg/kg or more, respectively, produced a marked increase in blood flow; vertebral blood flow showed the largest increase, followed in order by carotid and femoral blood flow; however, the data of vertebral blood flow for 2 showed no significant difference because of their large variances. Compounds 4 and 8 increased the three arterial blood flows almost to the same extent. For compound 5 the vertebral artery showed the most pronounced reaction, followed by the carotid and femoral arteries. Compounds 6 and 7 produced an effect similar to, but generally lower than, that of 3. Compound 9 markedly increased femoral arterial blood flow. Compound 10 did not increase blood flow in any of the three arteries. Diltiazem at 0.03 mg/kg or more caused an increase in blood flow: vertebral blood flow showed the largest increase, followed in order by carotid and femoral blood flow. Papaverine at 0.1 mg/kg or more increased the three arterial blood flows almost to the same extent. Thus,
inhibition of calcium flux through smooth muscle membrane; and compounds 6 and 7, synthesized on the basis of 3, showed similar effects. (3) compound 4 increased the blood flow of the three arteries to almost the same extent, suggesting its action to be similar to that of papaverine, which is said to inhibit non-selectively smooth muscle contraction through inhibitory effects on calcium flux and phosphodiesterase. Compound 8 receiving cleavage of the pyran ring of 4 showed a similar effect; and compound 9 in which a nitrogen atom was introduced into 8 markedly increased femoral arterial blood flow, (4) compound 1 increased blood flow of the cerebral cortex; this suggests the possibility for this compound to be used as a drug for improvement of cerebral circulation, and (5) thus, the action of compound 1 to blood pressure is different from that of 2 or 3, though 1 has a Ca²⁺ blocking action as part of its pharmacological actions. Therefore, compound 1 is considered to be different from diltiazem in its mode of action. There is the possibility that compound 1 is mixed with another compound that is different from compound 2 at 3' and 4' in its chemical structure. In this study, diltiazem was used as a control Ca²⁺ blocking drug. For elucidation the mechanism of action of compound 1, it is considered necessary to further study the comparison with dihydroxypropidine and verapamil Ca²⁺ blockers and to perform more detailed studies on the action to the cardiovascular system. The results of the pharmacological studies of coumarins 1—10 may account for the folk usage of *Peucedanum japonicum* Thunb.

**Experimental**

All melting points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 260-10 spectrometer, nuclear magnetic resonance (NMR) spectra with a Varian T-60 or a JEOL JNM-FX 100 spectrometer with tetramethylsilane as an internal standard and mass spectra (MS) with a JEOL JMS-D 300 spectrometer. Mallinkrodt silica gel (100 mesh) and Merck kieselgel G nach Stahl were used for column chromatography and thin layer chromatography (TLC), respectively. 3-Ketocarbonyl-5-hydroxy-4-methylcoumarin (11) Diethyl malonate (10.4 g) was added to a solution of 1.0 m tetrabutylammonium fluoride in tetrahydrofuran (THF; 19.5 ml), and the whole was concentrated under a vacuum at 40° C. 2,6-Dihydroxyacetophenone (5 g) was added to a solution of the residue in dry toluene (150 ml), then the mixture was refluxed overnight and concentrated under a vacuum. The residue was poured into water and extracted with chloroform. The organic layer was washed with dilute HCl and water, then dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 6.7 g (82.1%) of 11 as colorless crystals (methanol), mp 191—193°C. IR (KBr) cm⁻¹: 3310, 1730, 1685, 1600, 1500. NMR (CDCl₃) δ: 1.33 (3H, t, J = 8 Hz, -Me), 2.60 (3H, s, -Me), 4.30 (2H, q, J = 8 Hz, -CH₂), 5.60—6.73 (2H, m, aromatic H), 7.06 (1H, t, J = 8 Hz, aromatic H). MS m/z: Calcd for C₁₇H₁₈O₂ (M⁺): 248.0684. Found: 248.0684.

3-Carboxy-5-hydroxy-4-methylcoumarin (12) 10% KOH (104 ml) was added to a solution of 11 (3.47 g) in ethanol (104 ml), and the whole was refluxed for 3 h. The reaction mixture was poured into ice-water, then acidified with conc. HCl and extracted with ethyl acetate. The organic layer was washed with water, then dried and concentrated. The residue was recrystallized from methanol—benzene to yield 2.4 g (88.8%) of 12 as straw crystals, mp 229—230.5° C. IR (KBr) cm⁻¹: 3300, 1700, 1650, 1600, 1500. NMR (CDCl₃ + DMSO-d₆) δ: 2.68 (3H, s, -Me), 5.43 (2H, br,—OH and —CO₂H), 6.58 (1H, dd, J = 8, 2 Hz, aromatic H), 6.66 (1H, J = 8, 2 Hz, aromatic H), 7.16 (1H, t, J = 8 Hz, aromatic H), 7.50 (2H, aromatic H).

5-Hydroxy-4-methylcoumarin (13) Compound 12 (4.25 g) was heated at 240°C for 4 min and allowed to stand at room temperature. The resulted solid was recrystallized from ethyl acetate to give 3.09 g (90.7%) of 13 as light brown crystals, mp 266—268°C. IR (KBr) cm⁻¹: 3150, 1680, 1610, 1500. NMR (CDCl₃ + DMSO-d₆) δ: 2.56 (3H, d, J = 8 Hz, -Me), 3.18 (1H, br,—OH), 5.86 (1H, q, J = 1 Hz, olefine H), 6.48—6.66 (2H, m, aromatic H).

---

**Fig. 6. Effects of 1 on Cerebral Blood Flows in Rabbits**

- ○—○: control; ▲—▲: 30; ▼—▼: 100 mg/kg, 1 administration. Each point represents the mean ± S.E. of 5 to 6 experiments.
H). 7.08 (1H, dd, J = 8, 7 Hz). MS m/z Calc for C₄H₆O₂ (M⁺): 176.0474. Found: 176.0477.

4-Methyl-5-(2-methyl-3-butyra-2-xyloxy)coumarin (14) Sodium hydride (55%, 2.05 g) was added to a solution of 13 (3.0 g) in DMF (103 ml) with stirring at room temperature under a nitrogen atmosphere, and the whole was stirred for 18 h under the same conditions. The reaction mixture was poured into ice-water, acidified with cone. HCl, and extracted with ethyl acetate. The organic layer was washed with water, then dried and concentrated. The residue was subjected to silica gel chromatography. The benzene eluate of 14 as yellow crystals (ether-hexane), mp 102—103°C. IR (KBr) cm⁻¹: 3220, 1700, 1600, 1590. NMR (CDCl₃): δ: 1.73 (6H, s, —Me), 2.53 (3H, s, —Me), 2.62 (1H, s, acetylenic H), 5.96 (1H, m, olefinic H), 6.70—6.85 (1H, m, aromatic H), 7.18—7.20 (2H, m, aromatic H). MS m/z Calc for C₁₂H₁₀O₃ (M⁺): 242.0943. Found: 242.0954.

2,2,10-Trimethyl-2H thiophene-1,2:5,4-b' dipyrano-8-one (5) A solution of 14 (1.0 g) in N,N-dimethylacetamide (40 ml) was refluxed for 40 min. The reaction mixture was poured into ice-water, acidified with 10% HCl, and then extracted with ethyl acetate. The organic layer was washed with 10% HCl, 5% K₂CO₃, and brine, then dried and concentrated. The residue was recrystallized from ether–hexane to give 0.82 g (82.0%) of 8 as yellow crystals, mp 115—117°C. IR (Nujol) cm⁻¹: 1723, 1685, 1645, 1620, 1590, 1578. NMR (CDCl₃): δ: 1.47 (6H, s, —Me), 2.08 (3H, d, J = 1 Hz, —Me), 5.54 (1H, d, J = 10 Hz, olefinic H), 5.93 (1H, q, J = 1 Hz, olefinic H), 6.16 (1H, d, J = 10 Hz, olefinic H), 6.63 (1H, d, J = 8 Hz, aromatic H), 6.94 (1H, d, J = 8 Hz, aromatic H). MS m/z Calc for C₁₀H₈₂O₂ (M⁺): 321.1815. Found: 321.1825.

4-Methyl-7-((3-methyl-2-butenyl)oxy)coumarin (8) 4-Bromo-2-methyl-2-butenyl (1 ml) and anhydrous K₂CO₃ (400 mg) were added to a solution of 7-hydroxy-4-methylcoumarin (100 mg) in DMF (3 ml), and the whole was stirred at room temperature. The reaction mixture was poured into ice-water and extracted with ether. The organic layer was washed with water, dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 3.1 g (61.0%) of 8 as light yellow prisms (ether–hexane), mp 84—86°C. IR (Nujol) cm⁻¹: 1718, 1675, 1606, 1550, 1500. NMR (CDCl₃): δ: 1.78 (6H, s, —Me), 2.40 (3H, s, —Me), 4.58 (2H, d, J = 8 Hz, —CH₂), 5.48 (1H, t, J = 8 Hz, olefinic H), 6.16 (1H, s, olefinic H), 6.77—6.96 (2H, m, aromatic H). 7.50 (1H, d, J = 9 Hz, aromatic H). MS m/z Calc for C₁₀H₈₂O₂ (M⁺): 244.1100. Found: 244.1105.

7-(2-Dimethylaminoethoxy)-4-methylcoumarin Hydrochloride (9) 2-Di-methylaminoethyl chloride hydrochloride (288 mg) and anhydrous K₂CO₃ (414 mg) were added to a solution of 7-hydroxy-4-methylcoumarin (178 mg) in DMF (3 ml) and the whole was stirred overnight at room temperature. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with water, then dried and concentrated. The residue was recrystallized from ether–hexane to give 100 mg of 7-dimethylaminoethoxy-4-methylcoumarin as colorless prisms, mp 65—67°C. IR (Nujol) cm⁻¹: 1723, 1615, 1605, 1560, 1510. NMR (CDCl₃): δ: 2.36 (9H, s, —Me), 2.77 (2H, t, J = 10 Hz, —CH₂), 4.14 (2H, t, J = 10 Hz, —CH₂), 6.12 (1H, s, olefinic H), 6.82—6.99 (2H, m, aromatic H). 7.42 (1H, d, J = 13 Hz, aromatic H). MS m/z Calc for C₁₆H₁₄N₂O₂ (M⁺): 247.1209. Found: 247.1213. To a solution of 2-methylaminoethoxy-4-methylcoumarin (100 mg), conc. HCl (3 gt) was added and the whole was stirred at room temperature for 1 h. The reaction mixture was concentrated under a vacuum. The residue was recrystallized from ether to give 120 mg (49.1%) of 9 as colorless prisms, mp 224—225°C.

References