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# RORIPAMINE, A SULPHONYLALKYL AMINE FROM *RORIPPA INDICA*

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**Key Word Index**—*Rorippa indica*; Cruciferae; synthesis; roripamine; sulphonylalkyl amine.

**Abstract**—The chemical structure of roripamine, a novel sulphonylalkyl amine from the whole herb of *Rorippa indica* (L.) Hiern, has been elucidated by spectrometric and chemical studies. The structure of roripamine was also confirmed by synthesis.

## INTRODUCTION

A cruciferous weed species, *Rorippa indica* is a common perennial weed in Taiwan which grows strongly, and invades the territories of other plant species. As the weed exists in very dense and practically pure stands, this suggests that it may produce substances that are allelopathic to other surrounding plants.

Chemical studies of *Rorippa sylvestris* [1, 2] showed that salicylic, *p*-hydroxybenzoic, vanillic and syringic acids, 4-methoxyindole-3-acetonitrile and pyrocatechol together with hirsutin (8-methylsulphinyloctyl isothiocyanate) are present. The ethyl acetate extracts of *R. indica* [3] contained hirsutin, arabin, camelinin and three novel $\omega$-methylsulphonylalkyl isothiocyanates ($n$ = 8, 9 10). We have now studied the ethanol extract of the whole herb of *R. indica*, from which we have isolated a new methylsulphonylalkyl amine.

## RESULTS AND DISCUSSION

The whole herb of *R. indica* was repeatedly extracted with ethanol, and then partitioned with ethyl acetate and water. The latter layer was also partitioned with butanol. The butanol layer was repeatedly purified on Diaion HP-20 and Sephadex LH-20, giving a new sulphonyl alkyl amine, roripamine (**1**).

Roripamine (**1**) was obtained as pale yellow needles, mp 153–155°. It was deduced to have the molecular formula $C_{10}H_{23}SO_2N$ on the basis of a mass spectrum peak at $m/z$ 222 ($[M + 1]^+$, 32%). The presence of a sulphonyl moiety was confirmed by the IR absorption bands at 1310, 1290 and 1130 $cm^{-1}$, and an amino moiety by those at 3300, 1615, and 1525 $cm^{-1}$. The $^1H$ NMR spectrum revealed that **1** had one methyl group ($\delta$2.92, *s*), two triplet methylene groups [$\delta$2.72 and 3.07 (each 2H, *t*, $J$ = 6.8 Hz, H-9, H-1)], two multiplet methylene groups [$\delta$1.56 and 1.65 (each 2H, *m*, H-8, H-2)] and 10 protons ($\delta$1.26 *br s*). The irradiation of $\delta$1.56 and 1.65 simplified the signals at $\delta$2.72 and 3.07 to singlets, respectively. The acetylation of **1** with acetic anhydride gave a secondary acetamide (**2**) [mp 130–132°; 3320, 1625, 1535 $cm^{-1}$ (secondary amide), 1305, 1280, 1130 $cm^{-1}$ (sulphonyl); $\delta$1.94 (3H, *s*) and 5.51 (1H, *br s*, –NH, disappeared on $D_2O$ exchange)]. The $^{13}C$ NMR spectra of **1** and **2**, in addition to their mass spectral fragmentations, confirmed the structure of roripamine (**1**) as 9-methylsulphonylnonyl amine.

The proposed structure was further confirmed by synthesis. 2-(4-Pentenyl)sulpholane (**3**) was obtained from sulpholane by treatment with butyl lithium and 4-pentenyl tosylate in THF (Scheme 1). When 2-(4-pentenyl)sulpholane (**3**) was sonicated with UDP (ultrasonically dispersed potassium) in toluene and then MeI was added, the resulting mixture yielded 9-methylsulphonenon-2-ene (**4**) [4, 5]. On hydroboration and oxidation with hydroperoxide, **4** was converted to 9-methylsulphonenonanol-1 (**5**). 9-Methylsulphonenonal (**6**) was obtained from **5** by oxidizing with PCC in dichloromethane. Condensation of the aldehyde **6** with hydroxylamine in ethanol afforded oxime **7**. Finally, roripamine (**1**) was prepared from this oxime by catalytic hydrogenation with $PtO_2$ in acidic methanol solution.

## EXPERIMENTAL

*General.* Mps: uncorr.; $^1H$ (300 MHz) and $^{13}C$ (75 MHz) NMR recorded on Bruker 300 using TMS as int. standard; EIMS: Finnigan MAT TSQ-46C spectrometer, electron impact mode, 70 eV.

*Plant material.* Whole herbs of *Rorippa indica* (L.) Hiern were collected in Taipei. A voucher specimen has been deposited in the Herbarium of Taiwan University.

*Extraction and isolation of whole herb.* The pulverized, air-dried whole herb (10 kg) was soaked in EtOH (30 l) for a week. The EtOH extract was concd to give 150 g of a

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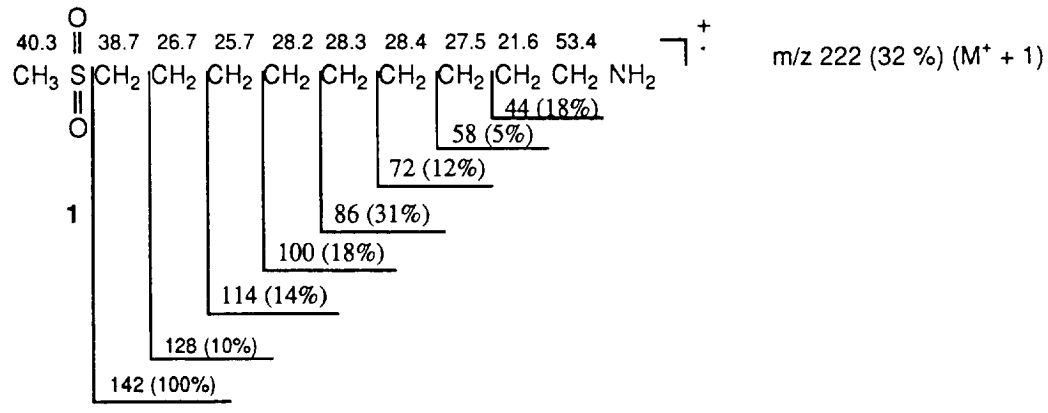


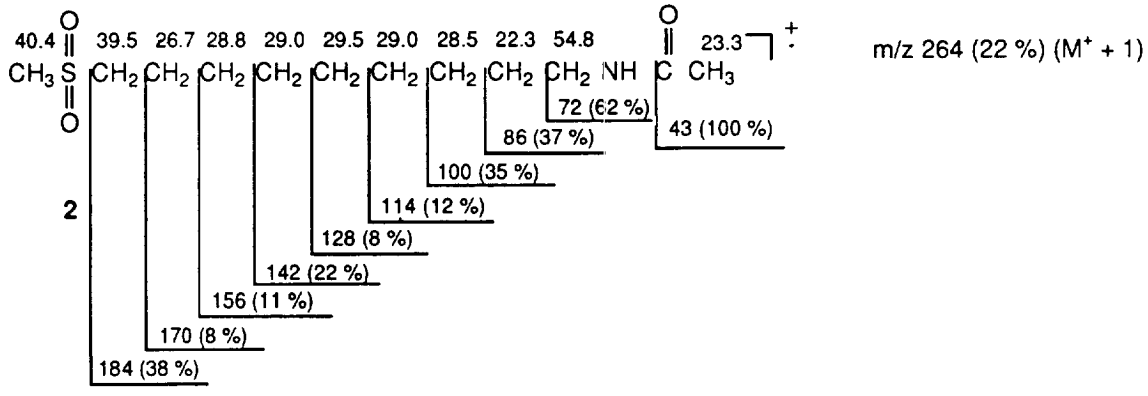


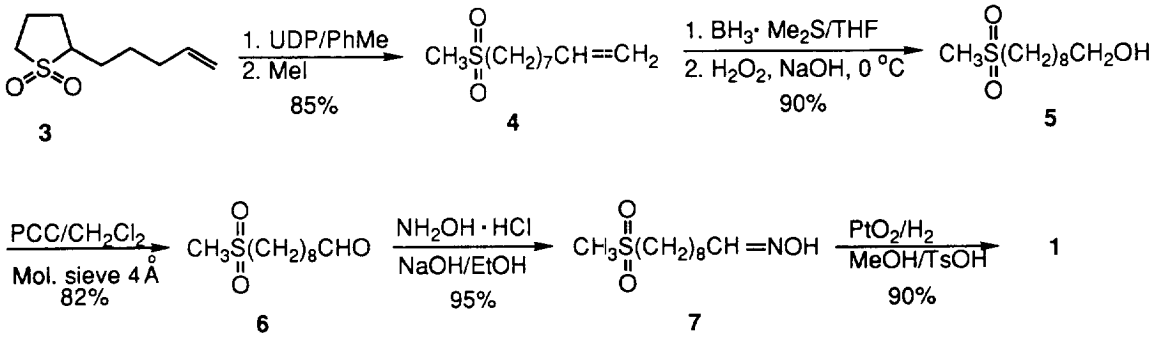


Scheme 1.

residue that was diluted with $H_2O$ and extracted (×2) with EtOAc. The $H_2O$ layer was partitioned with BuOH, and the BuOH extracts were subjected to chromotography on Diaion HP-20 and then on Sephadex LH-20 with MeOH and $H_2O$ as solvent. Roripamine (270 mg) was obtained from the MeOH–$H_2O$ (1:1) solvent system.

*Roripamine* (**1**). Mp 153–155°. IR $\nu_{max}$ $cm^{-1}$: 3300, 1615, 1575, 1525, 1310, 1290, 1270, 1130 and 970.

*Acetylation of roripamine* (**1**). Roripamine (**1**) (50 mg) was added to 2 ml $Ac_2O$ at ambient temp. for 30 min. And then 3 ml of 10% aq. NaOH soln was poured into the reaction mixt. dropwise and stirring continued at ambient temp. for 30 min. The reaction mixt. was poured into excess $H_2O$, and purified on silica gel to obtain amide **2** (95% yield) [mp: 130–132°; IR $\nu_{max}$ $cm^{-1}$: 3320, 1625, 1535, 1305, 1280, 1145, 1130. $^1$H NMR ($CDCl_3$): $\delta$ 1.23–1.45 (10H, *br s*), 1.62–1.88 (4H, *m*, H-2, H-8), 1.94 and 2.87 (each 3H, *s*), 2.97 (2H, *t*, $J$ = 6.8 Hz, H-9), 3.19 (2H, *q*, $J$ = 6.6 Hz, H-1), 5.51 (1H, *br s*, NH).

*Reductive bond cleavage of* 2-(4-*pentenyl*)*sulpholane* (**3**). 2-(4-Pentenyl)sulpholane (**3**) (300 mg, 2.5 mmol) in toluene was added dropwise to a suspension of UDP (7.5 mmol). Ultrasound irradiation was continued at 55° for 4 hr until complete consumption of the starting material. The ultrasound bath was removed and MeI (3 equiv.) was added and the resulting mixt. stirred at room temp. for another 30 min. When a ppt. appeared, satd $NH_4Cl$ (10 ml) was added; the product was extracted from the mixt. with $CHCl_3$ (3 × 20 ml), dried, concd and purified by silica gel CC to give **4**: oil; IR $\nu_{max}$ $cm^{-1}$:

3070, 3012, 1635, 1295, 1134, 961, 911 and 766. $^1$H NMR ($CDCl_3$): $\delta$1.20–1.50 (10H, *m*), 1.97–2.08 (2H, *m*), 2.82 (3H, *s*), 2.93 (2H, *t*, $J$ = 8.0 Hz), 4.83–5.0 (2H, *m*), 5.67–5.83 (1H, *m*). FAB-MS (positive) *m/z* (rel. int.): 205 ([M + 1]$^+$, 7), 140 (14), 135 (30), 124 (50), 107 (40), 95 (50), 82 (100) in 85% yield.

*Hydroboration of compound* **4**. $BH_3 \cdot Me_2S$ (2M, 0.1 ml, 0.6 mmol) was added dropwise to a soln of **4** (82 mg, 0.4 mmol) in 10 ml of tetrahydrofuran at 0–5°. The reaction mixt. was warmed up to ambient temp. for 2.5 hr under stirring. EtOH (2 ml) and 3 mol aq. NaOH (0.2 ml) were poured into the reaction mixt. and the reaction temp. reduced to 0°. Subsequently, 35% $H_2O_2$ (0.1 ml) was added and the mixt. stirred for 1.5 hr. After usual treatment, primary alcohol **5**: mp 123–124°; IR $\nu_{max}$ cm$^{-1}$: 3443, 1272, 1141, 1124, 1072, 970. $^1$H NMR ($CDCl_3$): $\delta$ 1.20–1.60 (12H, *m*), 1.77 (2H, *m*), 2.83 (3H, *s*), 2.93 (2H, *t*, $J$ = 7.6 Hz), 3.55 (2H, *t*, $J$ = 6.4 Hz). FAB-MS (positive) *m/z* (rel. int): 223 ([M + 1]$^+$, 8), 192 (10), 149 (35), 124 (40), 81 (100) was obtained in 90% yield.

*Oxidation of primary alcohol* **5** *with PCC*. Primary alcohol **5** (7.4 mg) in 2 ml of $CH_2Cl_2$ was added to a suspension of powdered 4 Å molecular sieve (0.5 g) and PCC (100 mg) in 2 ml $CH_2Cl_2$. The reaction mixt. was stirred at ambient temp. for 50 min. The suspension mixt. was diluted with $Et_2O$ (30 ml) and filtered with celite. Purification of the filtrate gave an aldehyde **6** (82% yield): oil; IR $\nu_{max}$ cm$^{-1}$: 2723, 1714, 1410, 1295, 1133, 962, 766. $^1$H NMR ($CDCl_3$): $\delta$1.20–1.70 (10H, *m*), 1.79 (2H, *m*), 2.37 (2H, *dt*, $J$ = 1.7, 7.2 Hz), 2.85 (3H, *s*), 2.95 (2H, *t*, $J$ = 7.7 Hz), 9.71 (1H, *t*, $J$ = 1.7 Hz). FAB-MS (positive) *m/z* (rel. int.): 221 ([M + 1]$^+$, 2), 192 (7), 177 (12), 149 (10), 122 (13), 97 (62), 81 (78), 56 (100).

*Reaction of hydroxyamine with aldehyde* **6**. Aldehyde **6** (51 mg) was dissolved in the mixt. of EtOH (4 ml) and $H_2O$ (1 ml) and to the soln $NH_2OH \cdot HCl$ (70 mg) and NaOH (120 mg) were added. The reaction mixt. was heated under reflux for 30 min. On cooling, the reaction was acidified with 1 M HCl, then extracted with EtOAc. The organic layer, purified by silica gel chromatography, afforded oxime **7** (95% yield): mp 78–80°; IR $\nu_{max}$ cm$^{-1}$: 3416, 3070, 1661, 1284, 1263, 1124, 968, 775. $^1$H NMR ($CDCl_3$): $\delta$1.23–1.57 (10H, *m*), 1.83 (2H, *m*), 2.35 (2H, *m*), 2.87 (3H, *s*), 2.98 (2H, *t*, $J$ = 8.1 Hz), 6.69 (1H, *t*, $J$ = 5.5 Hz). FAB-MS (positive) *m/z* (rel. int.): 236 ([M + 1]$^+$, 8), 218 (13), 177 (13), 156 (42), 138 (38), 97 (100).

*Catalytic hydrogenation of oxime* **7**. Oxime **7** (37 mg) and *p*-toluenesulphonic acid (10 mg) were dissolved in 10 ml of MeOH, and 10 mg of $PtO_2$ added and the mixture satd with $H_2$. After 10 hr, the catalyst was removed by filtration and washed several times with MeOH. After removal of MeOH, 30 ml of 1% aq. NaOH was added and then subsequently extracted with EtOAc. After purification, the organic layer gave roripamine (**1**) in 90% yield.

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## REFERENCES

1. Kawabata, J., Fukushi, Y., Hayashi, R., Suzuki, K., Mishima, Y., Yamane, A. and Mizutani, J. (1989) *Agric. Biol. Chem.* **53**, 3361.
2. Yamane, A., Nishimura, H. and Mizutani, J. (1992) *J. Chem. Ecol.* **18**, 683.
3. Yamane, A., Nishimura, H., Ogawa, J. and Mizutani, J. (1992) *J. Chem. Ecol.* **18**, 1941.
4. Chou, T. S., Hung, S. H., Peng, M. L. and Lee, S. J. (1991) *J. Chin. Chem. Soc.* **38**, 283.
5. Chou, T. S. and You, M. L. (1985) *Tetrahedron Letters* **37**, 4495.