A Rearrangement Route to Fenvaleric Acid

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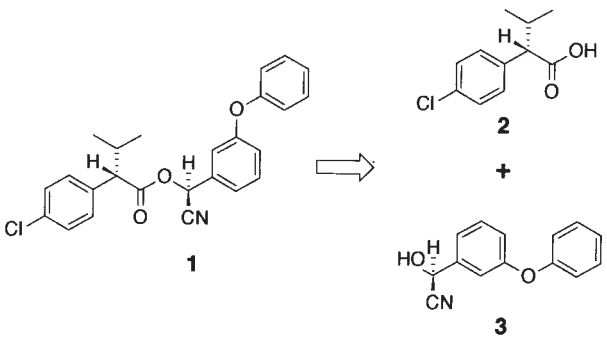
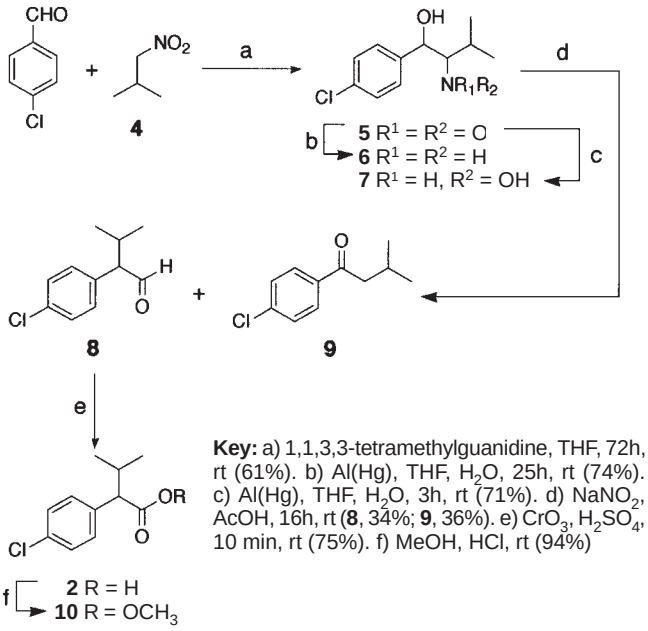
Abstract. (±)-Fenvaleric acid **2**, the key intermediate for the preparation of the pesticide esfenvalerate **1**, was prepared by a novel sequence which first involves the Henry reaction of 2-methyl-1-nitropropane and 4-chlorobenzaldehyde. The nitroaldol reaction provided nitroalcohol **5** which was then reduced to the corresponding aminoalcohol **6**. Submission of **6** to an aminopinacol rearrangement promoted by nitrous acid deamination then afforded aldehyde **8** through a 1,2-aryl shift. The product fenvaleric aldehyde **8** was then converted to the title compound **2** by a modified Jones oxidation.

Esfenvalerate, (*S*,*S*)-α-cyano-3-phenoxybenzyl-2-(4-chlorophenyl)-3-methylbutyrate (**1**), one of the most widely-used pesticides in the synthetic pyrethrin analog class, holds a prominent place in the agrochemical world [1]. Designated by Several trade names such as Sumicidin®, Sumi-alpha®, Asana XL®, Pydrin® and fenvalerate® [2], esfenvalerate is a broad-spectrum insecticide which exhibits limited mammalian toxicity and adequate stability in the environment [3]. Esfenvalerate has two chiral centers, thus allowing for the preparation of four possible stereoisomers, with the *(S,S)*-stereoisomer having the highest insecticidal activity [4]. Several routes have yielded racemic and stereochemically pure **1**, both in isotopically-labeled and unlabeled form. A simple retrosynthetic analysis, formally an ester cleavage, transforms **1** to 2-(4-chlorophenyl)-3-methylbutyric acid (fenvaleric acid) (**2**) and (α-cyano-3-phenoxybenzyl alcohol (**3**). (Scheme 1). Therefore, the majority of previous routes for the preparation of **1** resides in the synthesis of fenvaleric acid (**2**). Examples of previously-reported syntheses of **2** include alkylation of 4-chlorophenylacetonitrile with isopropyl halides [5] followed by hydrolysis and optical resolution [6], rhodium-catalyzed asymmetric hydroformylation reactions of 2-methyl-1-(4-chlorophenyl)propene followed by oxidation [7], asymmetric reduction of 3-methyl-2-chlorophenyl-2-butenoic acid [8] and asymmetic alkylation of 4-chlorophenylacetic acid with a chiral auxiliary [9]. Our interest in an alternative laboratory-scale synthesis of (±)-**2** emerges from the standpoint of evaluating potential prepa-rative routes for isotopic labeling as well as probing the utility of the Henry reaction in preparing small molecules of commercial interest. This report addresses a novel preparation of racemic **2** which utilizes the nitroaldol (Henry) reaction [10] and the classical aminopinacol rearrangement [11] as the key steps. Our synthesis of (±)-**2** (Scheme 2) commences with the reaction of 2-methyl-1-nitropropane **4**, freshly-prepared by the method of Kornblum [12], and 4-chlorobenzaldehyde thereby furnishing nitroalcohol **5**. The nitroaldol reaction required extended reaction times despite the usage of bases/reaction systems such as potassium fluoride/DMF, triethylamine/THF, sodium methoxide/methanol or the silyl nitronate of **4** [13]. Finally, the reaction of nitroalkane **4** and 4-chlorobenzaldehyde in the presence of a catalytic amount of 1,1,3,3-tetra-



Scheme 1 Retrosynthesis of esfenvalerate (**1**)



Key: a) 1,1,3,3-tetramethylguanidine, THF, 72h, rt (61%). b) Al(Hg), THF, H_2O, 25h, rt (74%). c) Al(Hg), THF, H_2O, 3h, rt (71%). d) $NaNO_2$, AcOH, 16h, rt (**8**, 34%; **9**, 36%). e) CrO_3, H_2SO_4, 10 min, rt (75%). f) MeOH, HCl, rt (94%)

Scheme 2 Synthesis of (±)-fenvaleric Acid (**2**) and its methyl ester (**10**)

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methylguanidine (TMG) [14] in anhydrous THF (72 h) gave a *threo/erythro* (3:1) mixture of nitroalcohols **5** in 61% yield after purification by silica gel flash column chromatography. The aldehyde and the more expensive nitroalkane coupling partner could be effectively recovered and resubmitted to the nitroaldol reaction. Reduction of **5** to aminoalcohol **6** was accomplished in 74% yield with aluminum amalgam (5 eq) in THF/H_2O (rt, 25 h) [15]. In contrast, allowing the reduction to proceed over three hours followed by workup and purification of the products by column chromatography resulted in a 71% yield of the corresponding hydroxylamine **7** as a consequence of incomplete reduction. The deamination-rearrangement of **6** using sodium nitrite in dilute acetic acid provided a mixture of aldehyde **8** (34%) and ketone **9** (36%). Both rearrangement products were separable by preparative thin-layer chromatography on silica gel. Aldehyde **8** arises from the well-studied 4-chlorophenyl migration [16] during semipinacol rearrangement while ketone **9** arises from the competing hydride shift [17]. The competition between hydride and phenyl migration has been the subject of several seminal papers dealing with migratory aptitudes in the classical pinacol and semi (amino-)pinacol rearrangements. Although our rearrangement employed the 3:1 mixture of *threo* and *erythro* diastereomeric amino alcohols and given that the migratory aptitude of the 4-chlorophenyl group ranges from 0.66 to 0.9 (phenyl=1) [18], our results were in accordance with the trends reported by Collins whereby a phenyl/hydrogen migration ratio in dilute acids ranges from 0.43–1.44 [19]. Interestingly, a simi-lar 4-chlorophenyl migration was employed in preparing optically active fenvaleric acid by treatment of a brominated chiral ketal derivative with silver ion [20]. Treatment of aldehyde **8** with Jones reagent (CrO_3/H_2SO_4/H_2O) followed by extractive workup and preparative TLC afforded the title carboxylic acid **2** (75%) as oil which slowly crystallized on standing. For comparison, a small sample of commercial **1** was saponified (NaOH/THF/H_2O/6h) thereby furnishing a sample of **2** after acidic workup and extractive isolation. Our synthetic **2** and its methyl ester **10** were identical in all respects (^{1}H and ^{13}C NMR, MS, FTIR and TLC mobility), save for optical purity, with the sample of **2** and its methyl ester derivative obtained from hydrolysis of commercially-available **1**.

In summary we have detailed a novel synthetic route to fenvaleric acid, an agrochemically-significant synthetic intermediate. The key carbon–carbon bond-forming step is the nitroaldol reaction while the key step in forming the final connectivity of the molecule was effected by the classical skeletal rearrangement afforded by the aminopinacol reaction. Although the yields of the individual steps were not optimized, the overall synthesis would be more serviceable for benchtop synthesis rather than on the multikilogram scale required by commercialization due to the compromised yields of aldehyde inherent in the rearrangement reaction. In terms of a new scheme for the preparation of isotopically-labeled fenvaleric acid, the nitroaldol/rearrangement route may be a welcome departure for the placement of ^{14}C or ^{13}C isotopes in positions alternate to those previously reported.

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Experimental

All reactions were conducted under an atmosphere of dry nitrogen unless otherwise noted. Where required, tetrahydrofuran and ether were distilled from sodium/benzophenone ketyl and acetone was distilled from $CaSO_4$. All other solvents were reagent grade and were used as received. Gravity-column chromatography was carried out using E. Merck silica gel 7734,70–230 mesh. Flash-column chromatographic separations [21] employed E. Merck silica gel 9385, 230–400 mesh. Analytical thin-layer chromatography was performed using glass-backed plates, E. Merck 5715 silica gel 60 F_{254}. Visualization of thin-layer chromatograms was accomplished by momentary immersion of the plate in a solution of 2% anisaldehyde in ethanol followed by heating with a heat gun or hot plate. ^{1}H and ^{13}C spectra were recorded with a Bruker AMX-500 instrument at 500.13 MHz and 125.77 MHz respectively, or on a Varian INOVA 300 Instrument at 299.95 MHz and 75.42 MHz respectively. All spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard. Carbon signals marked with an asterisk represent methyl and methine carbons as determined by APT experiments. Proton coupling constants are recorded in Hz. Infrared spectra (IR) were taken on a Mattson Instruments Galaxy 5000 or a Nicolet Impact 410 FI'IR as a neat film or KBr pellet and are expressed in cm^{-1}. Electron impact mass spectra of volatile compounds were recorded using a Hewlett-Packard 5890 Series II gas chromatograph equipped with a Hewlett-Packard 5971 quadrupole Mass Selective Detector and tuned against standard perfluorotributylamine. Elemental analyses were performed at Schwartzkopf Microanalytical Laboratory, Woodside, New York.

Threo- and erythro-1-(4-chlorophenyl)-2-nitro-3-methylpropanol (**5**)

To a solution of 4-chlorobenzaldehyde (1.2 g, 8.5 mmol) and 2-methyl-l-nitropropane **4** (2.57 g, 25.5 mmol) [12] in dry THF (4.5 mL) was added 1,1,3,3-tetramethylguanidine (289 µl, 2.5 mmol) by syringe. The resulting yellow-orange solution was stirred at room temperature for 72 h. The solution was then concentrated *in vacuo* to a yellow oil and directly flash-chromatographed on silica gel (hexanes/ethyl acetate, 4:1) to afford 1.24 g (61%, 91% corrected for recovered 4-chlorobenzaldehyde) of nitroalcohol **5** as a colorless oil. Immediately prior to spectral analysis a small amount of **5** was kugelrohr-distilled with a Büchi apparatus: B.p.$_{0.0.5}$ 159–160 °C. – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm (*threo*) = 7.2–7.4 (m, 4H, aromatic) 5.11 (t, J = 6.7 Hz, C2), 4.50 (dd, J = 6.4, 7.4, 1H, C1), 3.09 (d, J = 5.8 Hz, 1H, OH), 1.97 (oct, J = 6.7, 2.48, 1H, C3), 0.98 (dd, J = 6.7) 6H, 4-CH_3, 4'-CH_3. – ^{14}C (125.77 MHz, $CDCl_3$): δ/ppm = 137.3 (C4"), 134.6 (C1"), 129.1 (C3", C5")*, 128.0 (C2", C6")*, 98.2 (C2)*, 72.2 (C1)*, 28.7 (C3)*, 19.72 (C4') 17.0 (C4)*. (*erythro*) 7.2–7.4 (m, 4H, aromatic), 5.11 (t, J = 6.7 Hz, C2), 4.55 (dd, J = 5.1, 7.6, 1H, C1), 2.71 (br s, 1H, OH), 2.48 (d oct, J = 6.7, 6.9, 1H, C3), 1.01 (d, J = 6.9, 6H, 4-CH_3,4'CH_3). – ^{14}C (125.77 Hz, $CDCl_3$): δ/ppm = 138.0 (C4"), 134.4 (C1"), 128.7 (C3", C5")*, 128.3 (C2", C6")*, 97.3 (C2)*, 71.7 (C1)*, 28.5 (C3)*, 19.78 (C4')*, 16.8 (C4)*.

$C_{11}H_{14}ClNO_3$ (243.7)	Calcd:	C 54.22	H 5.79	N 5.75
	Found:	C 54.26	H 5.91	N 5.71.

Threo-and erythro-2-amino-l-chlorophenyl-3-methylpropanol (**6**)

Amalgamated aluminum coils were prepared by cutting 8× 20 mm strips of aluminum foil (156 mg, 1.16 mmol), winding the strips about a glass stirring rod into coils, washing the coils in ether followed by immersing (20 sec) into an agitated 2% aqueous solution of mercuric chloride (50 mL) then washing with ether (5 sec) with agitiation. Each coil was immediately added to a solution of nitroalcohol **5** (282 mg, 1.16 mmol) in THF (5.0 mL) and deionized water (0.31 mL). Stirring was continued for 25 hours. The gray suspension was filtered through a glass wool plug, concentrated *in vacuo* then flash-chromatographed ($CHCl_3$/MeOH, 9:1) to provide **6** (166.8 mg, 67%) as an oil. R_f = 0.06 ($CHCl_3$/MeOH, 4:1). – IR (KBr pellet): ν_{max}/cm^{-1} = 3373, 3238, 3028, 2930, 2852, 1602, 1494, 1454, 1047, 744, 698. – ^{1}H NMR (500 MHz, $CDCl_3$) (threo): δ/ppm = 7.1–7.3 (m, 4H, aromatic); 4.30 (d, J = 6.7, 1H, C1), 2.60 (br s, 3H, NH2, OH), 2.48 (dd, J = 4.6, 6.2, 1H, C2), 1.44 (d oct, J = 1.8, 6.7. 1H, C3), 0.82 (d, J = 6.7, 3H, C4). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 141.6 (C4"); 133.0 (C1"), 128.4 (C3", C5"), 127.9 (C2", C6"), 73.6 (C1)*, 62.6 (C2)*, 28.6 (C3)*, 20.6 (C4')*, 16.4(C4)*. – (*erythro*) ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.1–7.3 (m, 4H, aromatic), 4.30 (d, J = 6.7, 1H, C1), 2.60 (br s, 3H, NH_2, OH), 2.48 (dd, J = 4.6, 6.2, 1H, C2), 1.44 (d oct, J = 1.8, 6.7, 1H, C3), 0.82 (d, J = 6.7, 3H, C4). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 140.9 (C4"), 133.1 (C1"), 128.3 (C3", C5")*, 128.3 (C2", C6"), 74.1 (C1)*, 61.6 (C2)*, 28.6 (C3)*, 20.7 (C4')*, 16.8 (C4)*. – MS (ES+): *m*/*z* (%) = 214.2 (M+H).

Threo-and erythro-1-(4-chlorophenyl)-2-hydroxylamino-3-methylpropan-1-ol (**7**)

Treatment of **5** (177.2 mg, 0.73 mmol) with amalgamated aluminum coils (120.4 mg, 4.46 mmol) and THF/water (25:1, 5.2 mL) under the same reaction conditions except for an abbreviated reaction time (3 h) resulted in isolation of the hydroxylamine **7** (118.5 mg, 74%) after column chromatography on silica gel (chloroform/MeOH, 9:1). – IR (KBr pellet): ν_{max}/cm^{-1} = 3358, 3300, 2963, 2874, 1645, 1595, 1491, 1467, 1089. – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = (*threo*) 7.2–7.3 (m, 4H, aromatic), 5.52 (br s, 3H, NH + 2OH), 4.75 (d, J = 6.7, 1H, C1), 2.63 (dd, J = 5.3, 6.7, 1H, C2), 1.75 (oct, J = 6.5, 1H, C3), 0.94 (d, J = 6.9, 3H, C4'), 0.86 (d, J = 7.2, 3H, C4). – ^{13}C (125MHz, $CDCl_3$ (syn): δ/ppm = 140.9 (C4"), 133.4 (C1"), 128.7 (C3", C5")*, 128.0 (C2", C6")*, 74.3 (C1)*, 71.2 (C2)*, 27.0 (C3)*, 20.6 (C4')*, 18.3 (C4)*. (*erythro*) 7.2–7.3 (m, 4H, aromatic), 5.52 (br s, 3H, NH+2OH), 5.11 (d, J = 3.5, 1H, C1), 2.90 (dd, J = 3.7, 4.6, 1H, C2), 1.62 (d oct, J = 1.6, 6.9, 1H, C3), 0.84 (d, J = 6.6, 3H, C4), 0.83 (d, J = 6.5, 3H, C4); (anti) 140.3 (C4"), 132.8 (C1"), 128.4 (C3", C5")*, 127.5 (C2", C6")*, 72.2 (C1)*, 71.2 (C2)*, 26.0 (C3)*, 22.0 (C4')*, 18.4 (C4)*.

2-(4-Chlorophenyl)-3-methylbutanal (**8**) and *1-(4-chlorophenyl)-3-methylbutan-l-one* (**9**)

Acetic acid (0.25 mL, 4.33 mmol) was added to a solution of aminoalcohol **6** (9.3 mg, 0.044 mmol) and sodium nitrite (9.4 mg, 0.13 mmol) in water (0.25 mL). The effervescent yellow-orange solution was stirred for 2 h and an additional amount of sodium nitrite (9.3 mg, 0,13 mmol) was added. The solution was stirred at room temperature (16 h), sodium nitrite (9.3 mg, 0.13 mmol) was added, then stirring was continued at which time TLC analysis indicated complete consumption of **6**. The reaction mixture was carefully neutralized by slow addition of saturated sodium bicarbonate (2.0 mL) followed by extraction with hexane (5×2 mL). The combined extracts were dried over sodium sulfate, concentrated and the residue was purified by preparative TLC to afford 2.9 mg (34%) of aldehyde **8** [22]. R_f = 0.31 (hexane/EtOAc, 19:1). – IR (film): ν_{max}/cm^{-1} = 1962, 2930, 2874, 2715, 1724, 1493, 1467, 1091. – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 9.66 (d, J = 3.2, 1H, C<u>H</u>O), 7.32 (d, J = 8.5, 2H, aromatic), 7.11 (d, J = 8.5, 2H, aromatic) 3.16 (dd, J = 3.1, 9.4, 1H, C2), 2.36 (m, 1H, C3), 1.02 (d, J = 6.4, 3H, C4-CH_3), 0.74 (d, J = 6.6, 3H, C4'-CH_3). – MS (EI): *m*/*z* (%) = 198/196 (M+), 169/167, 156/1.54, 127/125 (100), 89, 55. The ketone rearrangement product **9** (3.1 mg, 36%) was isolated as a colorless oil: R_f = 0.42 (hexane/EtOAc, 9:1). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.87 (d, J = 8.5, 2H, aromatic), 7.41 (d, J = 8.5, 2H, aromatic), 2.78 (d, J = 6.6, C2), 2.25 (m, J = 6.4, 1H, C3), 0.96 (d, J = 6.1, C4-CH_3, C4'-CH_3). – MS (EI): *m*/*z* (%) = 184/182 (M–CH_3), 141/139 (100), 113/111, 85, 75, 50, 41, 27.

2-(4-Chlorophenyl)-3-methylbutanoic acid [**(±)-2**]

a) From aldehyde **8**: Chromic acid (15 µL of a 3.6M solution in aqueous 5.8M H_2SO_4) was added in portions (5 µL) until the orange color persisted at which time TLC analysis indicated complete consumption of the aldehyde **8**. The excess oxidant was decomposed with isopropanol to afford a green solution which was filtered through a small column packed with silica gel (50 mm) and eluted with EtOAc (5.0 mL). The filtrate was concentrated and purified by preparative TLC (hexane/EtOAc, 19:1) to provide acid **(±)-2** (75%) as a colorless oil which solidified on standing. R_f = 0.04 (hexane/EtOAc, 19:1). – IR (film): ν_{max}/cm^{-1} = 3000 (br), 3086, 3028, 2964, 2935, 2874, 1705, 1493, 1300, 1219. – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.26 (m, 4H, aromatic), 3.11 (d, J = 10.6, 1H, C2), 2.20 (dsept, J = 6.7, 10.9, 1H, C3), 1.05 (d, J = 6.5, 3H, C4-CH_3), 0.69 (d, J = 6.7, 3H, C4'-CH_3). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 178.9 (C1), 136.1 (C4"), 133.3 (C1"), 129.8 (C3")*, 128.6 (C2")*, 59.1 (C2)*, 31.6 (C3)*, 21.4 (C4)*, 20.0 (C4')*. – MS (ES-): *m*/*z* (%) = 211.3 (M-H).
b) From esfenvalerate **1**: Aqueous sodium hydroxide (0.15 mL, 20% solution, 0.92 mmol) was added to a solution of commercial Pestanal® (190 mg, 0.45 mmol) dissolved in THF (3.8 mL) The solution was stirred at room temperature for 6 h, extracted with ether (5 × 2 mL), acidified with concentrated HCI (1 mL) and re-extracted with ether (5 × 2 mL). The acidic extracts were dried over sodium sulfate and concentrated to afford **(±)-2** contaminated with *m*-phenoxybenzoic acid (3%), but otherwise spectrally identical with the synthetic material.

Methyl-2-(4-chlorophenyl)-3-methylbutanoate (**10**)

a) From synthetic (±)-fenvaleric acid: Saturated methanolic HCl, prepared by bubbling the dry gas from a lecture bottle through dry methanol (5 min) and cooling to room temperature, was added to synthetic **(±)-2** (1.0 mg, 4.7 mmol). The

solution was stirred at room temperature (3 h), carefully neutralized with solid sodium bicarbonate and diluted with ether (2 mL). The solution was dried over sodium sulfate and concentrated to afford racemic ester **10** as a colorless oil (1 mg, 94%): R_f = 0.37 (hexane/EtoAc, 9:1). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.25 (s, 4H, aromatic), 3.62 (s, 3H, OCH_3), 3.11 (d, J = 10.6, 1H, C2), 2.27 (dsept, J = 6.7, 10.6, 1H, C3), 1.00 (d, J = 6.5, 3H, C4-CH_3), 0.67 (d, J = 6.7, 3H, C4'-CH_3). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 174.1 (C1), 136.8 (C4"), 133.1 (C1"), 129.8 (C3")*, 128.6 (C2")*, 59.2 (C2)*, 51.8 (CH_3O)*, 32.0 (C3)*, 21.3 (C4)*, 20.1 (C4')*. – MS (EI): *m*/*z* (%) = 228, 226, 186 (32), 184 (100), 169, 167, 154, 152, 127, 127, 1 15, 89, 55.

b) From fenvaleric acid derived from commercial esfenvalerate: Saturated methanolic HCl, prepared as described above, was added to acid **2** (75.9 mg, 0.36 mmol) prepared by the saponification of commercial **1**. The reaction mixture was stirred at room temperature (16 h), diluted with ether (10 mL), washed with saturated sodium bicarbonate (2 × 10 mL) and dried over anhydrous sodium sulfate. Removal of the drying agent by filtration and concentration of the filtrate *in vacuo* provided the crude methyl ester **10** as an oil (R_f = 0.37; hexane/EtOAc, 9:1). The sample exhibited the same GC-MS. – ^{1}H and ^{13}C spectral characteristics as the material derived from **part a** as described above.

References

[1] L. G. Copping, Crop Protection Agents from Nature-Natural Products and Analogues The Royal Society of Chemistry: Cambridge, UK. 1998, pp 274

[2] Sumicidin® ,Sumi-Alpha® (Sumitomo Chemical Co.); Pydrine (Shell Development Co.); Asana XL® (DuPont Agricultural Products)

[3] R. L. Holmstead, D. G. Fullmer, L. O. Ruzo, J. Agric. Food Chem. **1978**, *26*, 9

[4] M. Miyakado, N. Ohno, Y. Okuno, M. Hirano, K. Fujimoto, H. Yoshioka, Agr. Biol. Chem. **1975**, *39*, 267; G. R. Cayley, B. W. Simpson, J. Chromatogr. **1986**, *356*, 123

[5] A. Yoshitake, H. Kanamaru, F. Shono, I. Nakatsukal J. Label. Comp. and Radiopharm. **1981**, 391; A. Q. Mi, Z. Y. Wang, Y. Z. Jiang, Tetrahedron: Asymmetry **1993**, *4*, 1957

[6] M. Inakagi, J. Hiratake, T. Nishioka, J. Oda, J. Org. Chem. **1992**, *57*, 5643; M. Ahmar, C. Girard, R. Bloch, Tetrahedron Lett. **1989**, *30*, 705

[7] C. Botteghi, D. Dallabona, S. Paganelli, M. Marchetti, B. Sechi, An. Quim. **1996**, *92*, 101

[8] T. Hayashi, N. Kawamura, Y. Ito, J. Am. Chem. Soc. **1987**, *109*, 7876

[9] F. Tanaka, M. Node, K. Tanaka, M. Mizuchi, S. Hosoi, J. Am. Chem. Soc. **1995**, *117*, 12159

[10] J. March, Advanced Organic Chemistry 4th Ed., John Wiley and Sons: New York 1992, p. 1073

[11] D. J. Coveny in, Comprehensive Organic Synthesis, B. M. Trost, Ed., Pergamon: Oxford 1991, Vol. 3, p. 777

[12] N. Komblum, J. W. Powers, J. Org. Chem. **1957**, *22*, 455; N. Kornblum, H. O. Larson, R. K. Blackwood, D. D. Mooberry, E. P. Olivetto, G. E. Graham, J. Am. Chem. Soc. **1956**, *78*, 1497

[13] M. Eyer, D. Seebach, J. Am. Chem. Soc. **1985**, *107*, 3601

[14] R. W. Fitch, F. A. Luzzio, Tetrahedron Lett. **1994**, *35*, 6013; D. Simoni, F. Invidiata, S. Manfredini, R. Ferroni, I. Lampronti, G. Pollini, Tetrahedron Lett. **1997**, *38*, 2749

[15] E. J. Corey, I. Vlattas, N. H. Andersen, K. Harding, J. Am. Chem. Soc. **1968**, *90*, 3245; M. Nakagawa, S. Kodato, K. Kakayama, T. Hino, Tetrahedron Lett. **1987**, *28*, 6281

[16] W. E. Bachmann, J. W. Ferguson, J. Am. Chem. Soc. **1934**, *56*, 2081

[17] W. Kirmse, W. Gruber, Chem. Ber. **1971**, *104*, 1789; W. Kirmse, H. Arold, Chem. Ber. **1971**, *104*, 1800

[18] D. Y. Curtin, M. C. Crew, J. Am. Chem. Soc. **1954**, *76*, 3719

[19] C. J. Collins, J. Am. Chem. Soc. **1955**, *77*, 5517

[20] G. Castaldi, S. Cavicchioli., C. Giordano, F. Uggeri, J. Org. Chem. **1987**, *52*, 3018

[21] W. C. Still, M. Kahn, A. Mitra, J. Org. Chem. **1978**, *43*, 2923

[22] Y. Tamaru, Y. Yamada, K. Inoue, Y. Yamamoto, Z. Yoshidia, J. Org. Chem. **1983**, *48*, 1286; I. Entwistle, P. Boehm, R. Johnstone, R. Telford, J. Chem Soc. Perkin Trans I **1980**, 27

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