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Versatile Amine-Promoted Mild Methanolysis of 3,5-Dinitrobenzoates and Its Application to the Synthesis of Colorado Potato Beetle Pheromone

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A mild deacylation method for 3,5-dinitrobenzoates using methanolic solutions of amines, such as dialkylamines, was developed. The method's versatility was confirmed by applying it to synthesizing a key intermediate for Colorado potato beetle pheromone.

Key words 3,5-dinitrobenzoate; amine-promoted methanolysis; selective deacylation; Colorado potato beetle pheromone

3,5-Dinitrobenzoates are typically crystalline compounds and are often used to confirm the structures of alcohols by X-ray crystallography.^{1–3} Some alcohols can be dinitrobenzoylated to improve their diastereomeric or enantiomeric purities by recrystallization.^{4–8} The resulting dinitrobenzoates are usually deacylated by alkaline solvolysis (a methanolic solution of K_2CO_3 or aqueous KOH).^{4–8} 3,5-Dinitrobenzoic acid has been used as a pro-nucleophile in the original Mitsunobu reaction⁹ and the catalytic Mitsunobu reaction.^{10,11} Thus, a mild deacylation method for dinitrobenzoates would be useful for synthesizing compounds such as natural products and biologically active compounds.

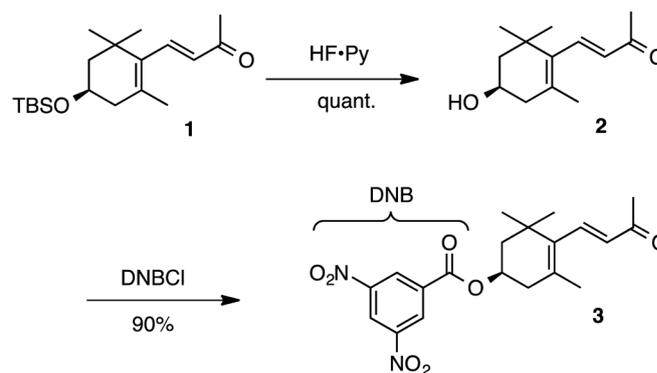
Recently, we found that methanolysis of the 3,5-dinitrobenzoate quickly proceeds in the presence of triethylamine in the total synthesis of lycopene-5,6-diols.⁸ Kobayashi and Acharya,¹² and Tono *et al.*¹³ reported that the dinitrobenzoates obtained by the Mitsunobu inversion of a secondary alcohols bearing macrocyclic lactone moieties were deacylated by treatment with a methanolic solution of triethylamine. These reports encouraged us to investigate versatility of this reaction. In the present work, we investigated the alcoholysis of dinitrobenzoates in the presence of various amines. Then, we applied our mild deacylation method in the efficient asymmetric synthesis of Colorado potato beetle (CPB) pheromone¹⁴ and its enantiomer.

Results and Discussion

Amine-Promoted Methanolysis of 3,5-Dinitrobenzoates The time course of the methanolysis in the presence of triethylamine (0.2–1.0 eq) of 3,5-dinitrobenzoate **3**, which was prepared from previously synthesized compound **1**¹⁵ (Chart 1), was monitored by HPLC (Fig. 1(a)). The conversions (%) of starting dinitrobenzoate **3** into alcohol **2** were calculated based on the peak areas and molar absorbance coefficients (ϵ) of **2** (2550) and **3** (9970) at a detection wavelength of 254 nm. The reaction proceeded even in the presence of a catalytic amount of triethylamine and the reaction rate increased with the molar equivalents of the amine. Next, we investigated the methanolysis of **3** in the presence of 0.5 eq of other amines (Fig. 1(b)). Reaction rates of ethylamine, diethylamine and diisopropylamine were almost identical, and those of ammonia,

triethylamine, 4-dimethylaminopyridine (DMAP) followed in this order. Methanolysis of **3** with 0.2 eq of diethylamine completed with a bit slower rate (99%: 4h) than that of 0.5 eq (99%: 1.5h). Interestingly, the rate of ethanolysis of **3** was much lower than that of methanolysis. A 1-mmol-scale methanolysis of **3** with 0.5 eq of diethylamine provided alcohol **2** in nearly quantitative isolated yield. This methanolysis procedure was convenient because extraction was not necessary and most of the methyl dinitrobenzoate by-product was removed by diluting the concentrated reaction mixture with ether and hexane followed by filtration.

Chloroacetates can be cleaved in the presence of other esters, such as acetates and benzoates, because of the large difference in the solvolysis rates.¹⁶ Thus, the time course of triethylamine-mediated (0.2, 0.5 eq) methanolysis of chloroacetate **4** was examined. The times for 50% conversion of 3,5-dinitrobenzoate **3** and chloroacetate **4** into deacylated product **2** showed that the reactivity of **3** was comparable to that of **4** (Table 1). Compound **8** was prepared and we examined the selective cleavage of the dinitrobenzoyl group in the presence of the acetyl (Ac) group on the primary allylic hydroxyl group (Chart 2). A methanolic solution of **8** was treated with diethylamine to provide chemoselectively deacylated alcohol **7** in high yield. Successful deacetylation of 3,5-dinitrobenzoate **10** of α -hydroxy ketone **9**¹⁷ without racemization reinforces the versatility of the reaction.

Chart 1. Synthesis of 3,5-Dinitrobenzoate **3**

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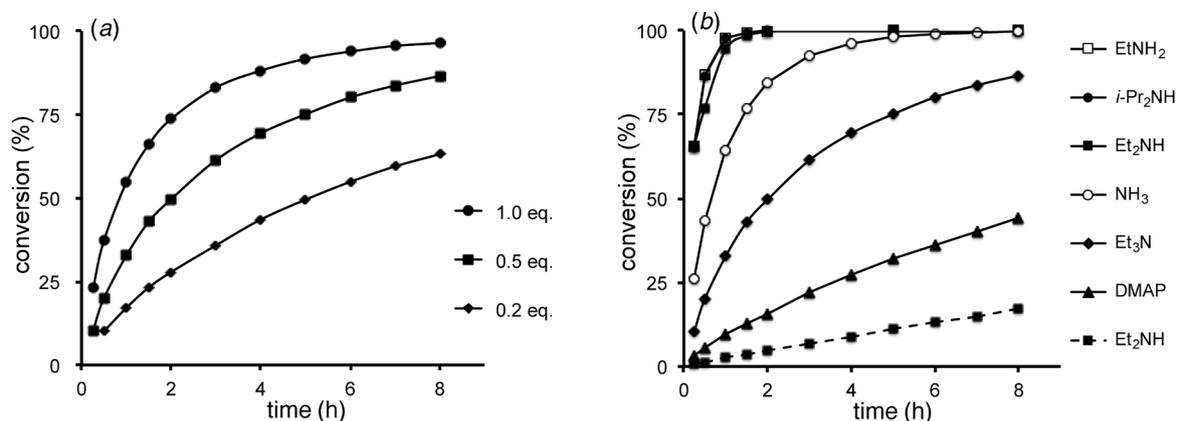


Fig. 1. Time Course of Alcoholysis of 3,5-Dinitrobenzoate 3

All experiments were conducted at room temperature (23–25°C) in a 0.02 M solution of 3 (0.1 mmol) in MeOH (—) or EtOH (----). (a) Treatment of 3 with 0.2–1.0 eq of Et₃N; (b) treatment of 3 with 0.5 eq of amine.

Table 1. Methanolysis of Compounds 3 and 4

Et₃N (0.2 or 0.5 eq)

MeOH (0.02 M), r.t.

2

3 R = DNB
4 R = COCH₂Cl

Substrate	Time for 50% conversion (h)	
	Et ₃ N (0.2 eq)	Et ₃ N (0.5 eq)
3	5.1	2.0
4	3.4	1.6

Synthesis of CPB Pheromone The CPB, *Leptinotarsa decemlineata*, is a severe defoliator of potatoes and related solanaceous plants worldwide.¹⁸⁾ The heavy use of synthetic insecticides for CPB control has led to insecticide resistance. The identification of the male-produced aggregation pheromone in CPBs, (3*S*)-1,3-dihydroxy-3,7-dimethyl-6-octen-2-one (**13a**), has made insecticide-free pest management of CPB possible. Preliminary bioassays revealed that (*S*)-**13a** attracted both sexes of *L. decemlineata*, whereas (*R*)-**13b** was inactive.¹⁴⁾ Thus, several enantioselective synthetic methods of the CPB pheromone have been developed.^{19–22)} In most cases, target compound **13** was derived through triol **14** by selective protection of the primary alcohol using *tert*-butyldiphenylsilyl chloride, oxidation with dimethyl sulfoxide, and deprotection.^{19,20,22)} The most recent synthesis²²⁾ derived **13** from triol **14**, which was prepared from geraniol in four steps by Sharpless asymmetric epoxidation, acetylation, treatment with aqueous perchloric acid in *N,N*-dimethylformamide, and deacylation using K₂CO₃ in methanol. To improve the enantiomeric purity, the CPB pheromone was converted into the crystalline 4-bromobenzoate derivative, recrystallized, and then hydrolyzed. However, the repeated protection and deprotection of the hydroxyl group is inefficient.

Recently, during the total synthesis of lycopene-5,6-diols,⁸⁾ we prepared enantiomerically pure 2,3-dihydroxyneryl 3,5-dinitrobenzoate **11a, b** via Sharpless asymmetric epoxidation of nerol followed by acidic hydrolysis (Chart 3). The dinitrobenzoyl group controlled the stereoselectivity in the epoxide ring

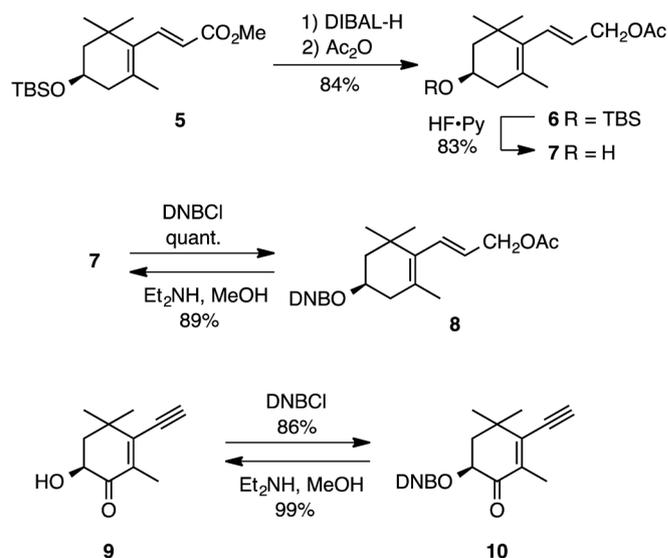
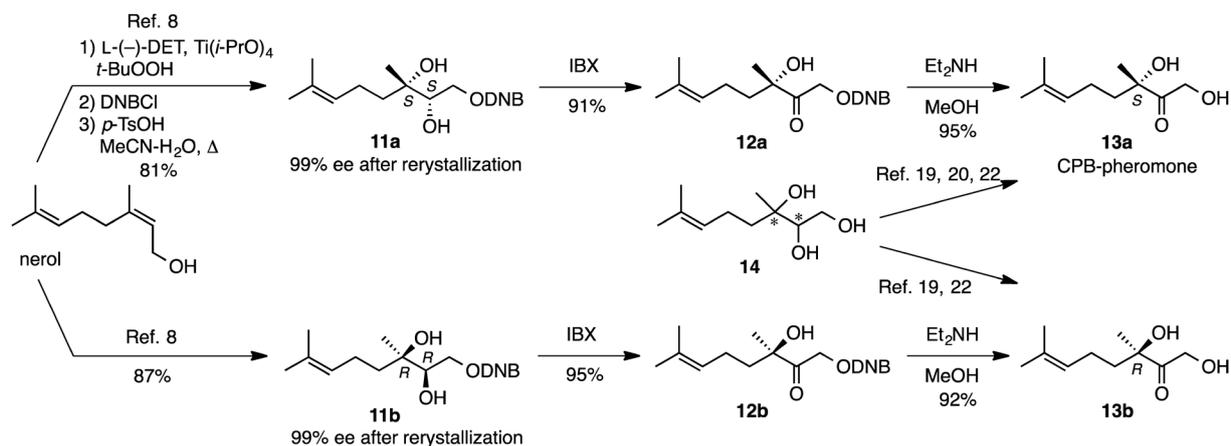


Chart 2. Preparation and Deacylation of Compounds 8 and 10

opening and improved the enantiomeric purities of products **11a, b** by making them easy to crystallize.

In the present work, we prepared CPB pheromone **13a** and its enantiomer **13b** from **11a, b** in two steps without triols **14**. **11a, b** was oxidized by 2-iodoxybenzoic acid (IBX) to provide ketones **12a, b** in high yields, which were then treated with diethylamine in methanol to give desired compounds **13a, b** in high yields. When benzoate **12a** was treated with aqueous KOH in methanol, deacylated compound **13a** was not obtained because of decomposition, indicating that dihydroxyketone **13** was unstable under the strongly basic conditions. The specific rotation values of **13a** and **b** were so small {**13a**: [α]_D²⁶ +3.6 (*c*=1.00, CHCl₃), **13b**: [α]_D²⁷ -2.4 (*c*=1.00, CHCl₃); lit.^{19,20,22)}: [α]_D²⁵ ±3.2 to ±4.0 (*c*=0.4 to 1.08, CHCl₃)} that their enantiomeric purities (**13a**: 97% enantiomeric excess (ee), **13b**: 98% ee) were directly confirmed by HPLC analysis (CHIRALPAK ID, Daicel; EtOH–hexane, 15 : 85).

In conclusion, the mild deacylation method of 3,5-dinitrobenzoates described here is promising as a versatile method for the synthesis of complex compounds such as natural products.

Chart 3. Synthesis of CPB Pheromone **13a** and Its Enantiomer **13b**

Experimental

General UV spectra were recorded on a JASCO V-650 instrument. IR spectra were measured on a Perkin-Elmer spectrum 100 Fourier transform (FT)-IR spectrometer. ¹H- and ¹³C-NMR spectra were determined on a Varian Gemini-300 superconducting FT-NMR spectrometer. The chemical shifts are expressed in ppm relative to tetramethylsilane ($\delta=0$) as internal standard for ¹H-NMR and CDCl₃ ($\delta=77.0$) for ¹³C-NMR. Mass spectra were taken on a Thermo Fisher Scientific Exactive spectrometer. Optical rotations were measured on a JASCO P-2200 polarimeter.

Flash column chromatography (CC) was performed on using Kanto Silica Gel 60N. HPLC analyses were performed on GL Sciences-GL7400 instrument with a photodiode array detector.

All operations were carried out under nitrogen or argon. Evaporation of the extract or the filtrate was carried out under reduced pressure. In solvent extraction procedure, organic layer was dried over anhydrous Na₂SO₄. Ether refers to diethyl ether, and hexane to *n*-hexane.

(E)-4-[(R)-4-Hydroxy-2,6,6-trimethylcyclohex-1-enyl]-but-3-en-2-one (2) HF·Pyridine (Py) (4 mL) was added in several portions to a solution of compound **1**¹⁵ (987 mg, 3.06 mmol) in tetrahydrofuran (THF) (10 mL) at 0°C. After being stirred at 0°C for 40 min, the reaction mixture was diluted with AcOEt, washed successively with brine, saturated aqueous NaHCO₃, and then brine. Evaporation of the dried solution gave a residue, which was purified by flash CC (acetone–hexane, 3 : 7) to afford compound **2** (638 mg, quant.) as a colorless oil: $[\alpha]_D^{23} -87.8$ ($c=1.01$, CHCl₃). IR (CHCl₃) cm⁻¹: 3606 and 3460 (OH), 1668 (CO), 1605 (C=C). UV λ_{max} (MeOH) nm (ϵ): 291 (9560). ¹H-NMR (300 MHz, CDCl₃) δ : 1.11 and 1.12 (each 3H, s, *gem*-CH₃), 1.49 (1H, t, $J=12$ Hz, 5'-H), 1.71 (1H, d, $J=4.5$ Hz, OH), 1.77 (3H, s, 2'-CH₃), 1.78 (1H, ddd, $J=12, 3.5, 2$ Hz, 5'-H), 2.09 (1H, brdd, $J=17, 9.5$ Hz, 3'-H), 2.30 (3H, s, CH₃CO), 2.43 (1H, brdd, $J=17, 5.5$ Hz, 3'-H), 4.00 (1H, m, 4'-H), 6.10 (1H, d, $J=16.5$ Hz, 3-H), 7.19 (1H, brd, $J=16.5$ Hz, 4-H). ¹³C-NMR (75 MHz, CDCl₃) δ : 21.55, 27.27, 28.53, 30.04, 36.87, 42.73, 48.37, 64.45, 132.28, 132.32, 135.58, 142.33, 198.55. High resolution (HR)-MS (electrospray ionization (ESI)) m/z Calcd for C₁₃H₂₀O₂Na [M+Na]⁺ 231.1356. Found 231.1354.

(R)-3,5,5-Trimethyl-4-[(E)-3-oxobut-1-enyl]cyclohex-3-enyl 3,5-Dinitrobenzoate (3) To a stirred solution of

compound **2** (1.43 g, 6.87 mmol), Et₃N (1.44 mL, 10.4 mmol) and DMAP (42 mg, 0.34 mmol) in dry CH₂Cl₂ (35 mL) was added 3,5-dinitrobenzoyl chloride (1.59 g, 6.89 mmol) at 0°C and the mixture was stirred at 0°C for a further 60 min. After the reaction was quenched by addition of saturated aqueous NH₄Cl, CH₂Cl₂ was evaporated off. The resulting mixture was diluted with AcOEt and washed with brine. The organic layer was dried and evaporated to give a residue, which was purified by flash CC (AcOEt–hexane–CH₂Cl₂, 1 : 5 : 3) to provide compound **3** (2.48 g, 90%) as a colorless solid: mp 102–105°C. $[\alpha]_D^{23} -56.9$ ($c=1.00$, CHCl₃). IR (CHCl₃) cm⁻¹: 1729 and 1670 (CO), 1628 and 1607 (C=C), 1549 and 1345 (NO₂). UV λ_{max} (MeOH) nm (ϵ): 209 (37000), 285 (11300). ¹H-NMR (300 MHz, CDCl₃) δ : 1.19 and 1.24 (each 3H, s, *gem*-CH₃), 1.83 (3H, s, 3-CH₃), 1.84 (1H, t, $J=12$ Hz, 6-H), 2.02 (1H, ddd, $J=12, 4, 2$ Hz, 6-H), 2.34 (3H, s, CH₃CO), 2.40 (1H, brdd, $J=17.5, 10$ Hz, 2-H), 2.68 (1H, brdd, $J=17.5, 5.5$ Hz, 2-H), 5.42 (1H, m, 1-H), 6.16 (1H, d, $J=16.5$ Hz, 2'-H), 7.22 (1H, brd, $J=16.5$ Hz, 1'-H), 9.16 (2H, d, $J=2.5$ Hz, ArH), 9.24 (1H, t, $J=2.5$ Hz, ArH). ¹³C-NMR (75 MHz, CDCl₃) δ : 21.41, 27.46, 28.35, 29.85, 36.72, 38.42, 43.85, 71.07, 122.33, 129.35 (C×2), 130.36, 132.89, 134.19, 136.01, 141.47, 148.65 (C×2), 162.07, 198.22. HR-MS (ESI) m/z Calcd for C₂₀H₂₂O₇N₂Na [M+Na]⁺ 425.1319. Found 425.1320.

Time Course of Alcoholysis of 3,5-Dinitrobenzoate 3 (Fig. 1) Each amine (1.0 M in MeOH; 20 μ L, 0.02 mmol to 100 μ L, 0.1 mmol) was added to a stirred solution of compound **3** (40.0 mg, 0.1 mmol) in MeOH or EtOH (5.0 mL). The reaction was monitored by HPLC [LiChrosorb CN 0.46×25 cm (Merck), AcOEt–hexane (3 : 7), 1.0 mL/min, 254 nm (detect.); methyl and ethyl 3,5-dinitrobenzoate: 4.0 min, **3**: 5.1 min, **2**: 6.1 min]. Conversions (%) of compound **3** into compound **2** were calculated as shown in the following equation.

$$\text{Conversion (\%)} = \frac{\frac{\text{peak area of 3}}{9970 (\epsilon \text{ at } 254 \text{ nm of 3})}}{\frac{\text{peak area of 3}}{9970} + \frac{\text{peak area of 2}}{2550 (\epsilon \text{ at } 254 \text{ nm of 2})}} \times 100$$

Et₂NH-Promoted Methanolysis of 3,5-Dinitrobenzoate 3 To a stirred solution of compound **3** (402 mg, 1.00 mmol) in THF (1 mL) and MeOH (30 mL) was added Et₂NH (1.0 M in MeOH; 0.5 mL, 0.5 mmol) at room temperature (r.t.). After

being stirred at r.t. for 1 h, MeOH was evaporated off. Ether (10 mL) and hexane (10 mL) were added to the resulting residue and the precipitates were filtered off. The filtrate was concentrated to give a residue, which was purified by flash CC (acetone–hexane–CH₂Cl₂, 1:2:2) to yield compound **2** (208 mg, quant.) as a colorless oil.

(R)-3,5,5-Trimethyl-4-[(E)-3-oxobut-1-en-1-yl]cyclohex-3-enyl 2-Chloroacetate (4) To a stirred solution of compound **2** (823 mg, 3.95 mmol), Et₃N (0.82 mL, 5.89 mmol) and DMAP (24 mg, 0.20 mmol) in dry CH₂Cl₂ (15 mL) was added slowly chloroacetyl chloride (0.38 mL, 4.78 mmol) at 0°C. After being stirred at 0°C for 1 h, the mixture was quenched by addition of saturated aqueous NH₄Cl and extracted with AcOEt. The extracts were washed with brine, dried and evaporated to give a residue, which was purified by flash CC (AcOEt–hexane, 1:2) to provide compound **4** (825 mg, 73%) as a colorless solid: mp 75–77°C. [α]_D²⁰ –60.9 (*c*=0.98, CHCl₃). IR (CHCl₃) cm⁻¹: 1749, 1687sh and 1669 (CO), 1607 (C=C). UV λ_{\max} (MeOH) nm (ϵ): 218 (7800), 287 (9700). ¹H-NMR (300 MHz, CDCl₃) δ : 1.12 and 1.16 (each 3H, s, *gem*-CH₃), 1.65 (1H, t, *J*=12 Hz, 6-H), 1.77 (3H, s, 3-CH₃), 1.85 (1H, ddd, *J*=12, 3.5, 2 Hz, 6-H), 2.21 (1H, brdd, *J*=17, 9.5 Hz, 2-H), 2.31 (3H, s, CH₂CO), 2.54 (1H, brdd, *J*=17, 5.5 Hz, 2-H), 5.15 (1H, m, 1-H), 6.12 (1H, d, *J*=16.5 Hz, 2'-H), 7.19 (1H, brd, *J*=16.5 Hz, 1'-H). ¹³C-NMR (75 MHz, CDCl₃) δ : 21.40, 27.42, 28.30, 29.76, 36.49, 38.28, 41.09, 43.58, 70.04, 130.76, 132.68, 135.75, 141.70, 166.93, 198.38. HR-MS (ESI) *m/z* Calcd for C₁₅H₂₂O₃Cl [M+H]⁺ 285.1252 and 287.1223. Found 285.1252 and 287.1221.

Time Course of Et₃N-Promoted Methanolysis of Chloroacetate 4 (Table 1) In the same manner as described for time course of alcoholysis of 3,5-dinitrobenzoate **3**, a solution of compound **4** (28.5 mg, 0.1 mmol) in MeOH (5.0 mL) was treated with Et₃N. The reaction was monitored by HPLC [LiChrosorb CN 0.46×25 cm (Merck), AcOEt–hexane (3:7), 1.0 mL/min, 254 nm (detect)]; **4** (ϵ at 254 nm: 3080): 4.2 min, **2** (ϵ at 254 nm: 2550): 6.1 min].

(E)-3-[(R)-4-tert-Butyldimethylsilyloxy(TBS)-2,6,6-trimethylcyclohex-1-enyl]allyl Acetate (6) To a solution of compound **5**¹⁵ (1.50 g, 4.43 mmol) in dry ether (30 mL) was added diisobutylaluminum hydride (DIBAL-H) (1.0 M in hexane; 9.8 mL, 9.8 mmol) at 0°C and the mixture was stirred at 0°C for 10 min. Excess DIBAL-H was destroyed by the addition of moist silica gel (SiO₂–H₂O, 5:1) and the mixture was filtered through Celite. The filtrate was dried and evaporated to give the crude alcohol, which was dissolved in dry CH₂Cl₂ (10 mL) and Et₃N (3.1 mL, 22.3 mmol), DMAP (54 mg, 0.44 mmol) and Ac₂O (0.84 mL, 8.89 mmol) were added to it. After being stirred at r.t. for 20 min, the reaction mixture was diluted with AcOEt and washed with brine. The organic layer was dried and evaporated to give a residue, which was purified by flash CC (AcOEt–hexane, 15:85) to give compound **6** (1.31 g, 84% from **5**) as a colorless oil: [α]_D²⁵ –77.5 (*c*=0.94, CHCl₃). IR (CHCl₃) cm⁻¹: 1733 (CO). ¹H-NMR (300 MHz, DCl₃) δ : 0.78 (6H, s, SiCH₃×2), 0.90 (9H, s, *tert*-Bu), 1.01 and 1.03 (each 3H, s, *gem*-CH₃), 1.47 (1H, t, *J*=12 Hz, 5'-H), 1.65 (1H, ddd, *J*=12, 3.5, 2 Hz, 5'-H), 1.67 (3H, s, 2'-CH₃), 2.04 (1H, brdd, *J*=17, 9.5 Hz, 3'-H), 2.07 (3H, s, CH₃COO), 2.20 (1H, brdd, *J*=17, 5.5 Hz, 3'-H), 3.93 (1H, m, 4'-H), 4.61 (2H, dd, *J*=6.5, 1 Hz, 1-H₂), 5.52 (1H, tt, *J*=16, 6.5 Hz, 2-H), 6.13 (1H, brd, *J*=16 Hz, 3-H). ¹³C-NMR (75 MHz, CDCl₃) δ : –4.60

(C×2), 18.21, 21.00, 21.20, 25.91 (C×3), 28.25, 29.93, 36.64, 42.71, 48.56, 65.44, 65.52, 127.29, 127.65, 132.15, 136.02, 170.84. HR-MS (ESI) *m/z* Calcd for C₂₀H₃₆O₃NaSi [M+Na]⁺ 375.2326. Found 375.2331.

(E)-3-[(R)-4-Hydroxy-2,6,6-trimethylcyclohex-1-enyl]-allyl Acetate (7) In the same manner as described for the preparation of compound **2**, desilylation of compound **6** (1.20 g, 3.40 mmol) gave crude products, which were purified by flash CC (acetone–hexane, 3:7) to provide compound **7** (677 mg, 83%) as a colorless oil: [α]_D²⁴ –116.3 (*c*=1.06, CHCl₃). IR (CHCl₃) cm⁻¹: 3606 and 3453 (OH), 1732 (CO). ¹H-NMR (300 MHz, CDCl₃) δ : 1.03 and 1.04 (each 3H, s, *gem*-CH₃), 1.44 (1H, t, *J*=12 Hz, 5'-H), 1.46 (1H, brs, OH), 1.68 (3H, s, 2'-CH₃), 1.75 (1H, ddd, *J*=12, 3.5, 2 Hz, 5'-H), 2.00 (1H, brdd, *J*=17, 9.5 Hz, 3'-H), 2.07 (3H, s, CH₃COO), 2.34 (1H, brdd, *J*=17, 5.5 Hz, 3'-H), 3.97 (1H, m, 4'-H), 4.60 (2H, dd, *J*=6.5, 1 Hz, 1-H₂), 5.51 (1H, dt, *J*=16, 6.5 Hz, 2-H), 6.11 (1H, brd, *J*=16 Hz, 3-H). ¹³C-NMR (75 MHz, CDCl₃) δ : 21.00, 21.18, 28.36, 29.95, 36.73, 42.17, 48.19, 64.96, 65.38, 126.64, 127.92, 131.94, 136.30, 170.87. HR-MS (ESI) *m/z* Calcd for C₁₄H₂₂O₃Na [M+Na]⁺ 261.1461. Found 261.1463.

(R)-4-[(E)-3-Acetoxyprop-1-enyl]-3,5,5-trimethylcyclohex-3-enyl 3,5-Dinitrobenzoate (8) In the same manner as described for the preparation of compound **3**, benzylation of compound **7** (614 mg, 2.58 mmol) gave crude products, which were purified by flash CC (AcOEt–hexane–CH₂Cl₂, 1:5:3) to provide compound **8** (1.12 g, quant.) as a pale yellow solid: mp 77–80°C. [α]_D²⁴ –71.5 (*c*=1.02, CHCl₃). IR (CHCl₃) cm⁻¹: 1729 (CO), 1548 and 1345 (NO₂). ¹H-NMR (300 MHz, CDCl₃) δ : 1.12 and 1.17 (each 3H, s, *gem*-CH₃), 1.75 (3H, s, 3-CH₃), 1.80 (1H, t, *J*=12 Hz, 6-H), 1.97 (1H, ddd, *J*=12, 3.5, 1.5 Hz, 6-H), 2.10 (3H, s, CH₃COO), 2.34 (1H, brdd, *J*=16.5, 9.5 Hz, 2-H), 2.59 (1H, brdd, *J*=16.5, 6 Hz, 2-H), 4.65 (2H, d, *J*=6.5 Hz, 3'-H₂), 5.41 (1H, m, 1-H), 5.59 (1H, dt, *J*=16, 6.5 Hz, 2'-H), 6.16 (1H, brd, *J*=16 Hz, 1'-H), 9.16 (2H, d, *J*=2 Hz, ArH), 9.23 (1H, t, *J*=2 Hz, ArH). ¹³C-NMR (75 MHz, CDCl₃) δ : 20.94, 21.04, 28.12, 29.69, 36.54, 37.84, 43.63, 65.13, 71.63, 122.22, 125.46, 128.56, 129.33 (C×2), 131.16, 134.34, 136.71, 148.59 (C×2), 162.08, 170.77. HR-MS (ESI) *m/z* Calcd for C₂₁H₂₄O₈N₂Na [M+Na]⁺ 455.1425. Found 455.1427.

Et₂NH-Promoted Methanolysis of 3,5-Dinitrobenzoate 8 In the same manner as described for Et₂NH-promoted methanolysis of 3,5-dinitrobenzoate **3**, methanolysis of compound **8** (200 mg, 0.46 mmol) gave the crude products, which were purified by flash CC (acetone–hexane–CH₂Cl₂, 2:9:9) to yield compound **2** (98 mg, 89%) as a colorless oil.

(S)-4-Ethynyl-3,5,5-trimethyl-2-oxocyclohex-3-enyl 3,5-Dinitrobenzoate (10) In the same manner as described for the preparation of compound **3**, benzylation of compound **9** (1.23 g, 6.90 mmol) gave crude products, which were purified by flash CC (AcOEt–hexane, 3:7) to provide compound **10** (2.21 g, 86%) as a colorless solid: mp 133–134°C. [α]_D²⁵ –166.3 (*c*=0.93, CHCl₃). IR (CHCl₃) cm⁻¹: 3302 (≡C–H), 2092 (C≡C), 1742 and 1689 (CO), 1628 (C=C), 1549 and 1345 (NO₂). ¹H-NMR (300 MHz, CDCl₃) δ : 1.41 and 1.47 (each 3H, s, *gem*-CH₃), 2.03 (3H, s, 3-CH₃), 2.27 (1H, dd, *J*=13, 7 Hz, 6-H), 2.33 (1H, t, *J*=13 Hz, 6-H), 3.88 (1H, s, ≡C–H), 5.82 (1H, dd, *J*=13, 7 Hz, 1-H), 9.20 (2H, d, *J*=2.5 Hz, ArH), 9.25 (1H, t, *J*=2.5 Hz, ArH). ¹³C-NMR (75 MHz, CDCl₃) δ : 14.37, 25.91, 30.48, 36.87, 41.20, 73.24, 79.66, 93.37, 122.59, 129.68 (C×2), 133.44, 137.44, 145.19, 148.63 (C×2), 161.87,

191.79. HR-MS (ESI) m/z Calcd for $C_{18}H_{16}O_7N_2Na$ $[M+Na]^+$ 395.0850. Found 395.0850.

Et₂NH-Promoted Methanolysis of 3,5-Dinitrobenzoate 10 In the same manner as described for Et₂NH-promoted methanolysis of 3,5-dinitrobenzoate **3**, methanolysis of compound **10** (372 mg, 1.00 mmol) gave the crude products, which were purified by flash CC (acetone–hexane–CH₂Cl₂, 1:6:3) to yield compound **9** (176 mg, 99%) as a colorless solid. ¹H-NMR data were identical with those previously reported.¹⁷⁾ The enantiomeric purity was confirmed (>99% ee) by chiral HPLC [CHIRALPAK IC 0.46×25 cm (Daicel), EtOH–hexane (5:95), 1.0 mL/min, 27°C, 267 nm (detect.); **9**: 11.13 min, enantiomer of **9**: 12.69 min]; HR-MS (ESI) m/z Calcd for $C_{11}H_{14}O_2Na$ $[M+Na]^+$ 201.0886. Found 201.0885.

(S)-3-Hydroxy-3,7-dimethyl-2-oxooct-6-enyl 3,5-Dinitrobenzoate (12a) To a solution of the compound **11a**⁸⁾ (1.00 g, 2.62 mmol) in dry THF (7.7 mL) and dry dimethylsulfoxide (7.7 mL) was added IBX (2.20 g, 7.86 mmol) in one portion and the reaction mixture was heated at 50°C for 1 h under stirring. After cooling, water (15 mL) was added to the mixture and the precipitates were filtered off and washed with AcOEt. The filtrate was washed with brine, dried and evaporated to give a residue, which was purified by flash CC (AcOEt–hexane, 3:7) to yield the ketone **12a** (908 mg, 91%) as a pale yellow viscous oil: $[\alpha]_D^{22}$ –23.1 ($c=0.99$, CHCl₃). IR (CHCl₃) cm^{-1} : 3605 and 3510 (OH), 1749 and 1732 (split.) (CO), 1550 and 1345 (NO₂). ¹H-NMR (300 MHz, CDCl₃) δ : 1.46 (3H, s, 3-CH₃), 1.65 and 1.71 (each 3H, s, *gem*-CH₃), 1.74 and 1.91 (each 1H, ddd, $J=14, 9.5, 6$ Hz, 4-H₂), 1.99–2.22 (2H, m, 5-H₂), 2.78 (1H, s, OH), 5.12 (1H, tsept, $J=7, 1$ Hz, 6-H), 5.34 and 5.41 (each 1H, d, $J=17.5$ Hz, 1-H₂), 9.22 (2H, d, $J=2$ Hz, ArH), 9.26 (1H, t, $J=2$ Hz, ArH). ¹³C-NMR (75 MHz, CDCl₃) δ : 17.73, 22.15, 25.68, 26.01, 39.69, 67.36, 79.53, 122.69, 123.04, 129.71 (C×2), 133.03, 133.49, 148.65 (C×2), 162.00, 200.26. HR-MS (ESI) m/z Calcd for $C_{17}H_{19}O_8N_2$ $[M-H]^-$ 379.1147. Found 379.1151.

(R)-12b

In the same manner as described above, compound **11b**⁸⁾ (1.00 g, 2.62 mmol) was converted into (R)-**12b** (949 mg, 95%) as a pale yellow viscous oil; $[\alpha]_D^{24}$ +17.6 ($c=1.02$, CHCl₃). HR-MS (ESI) m/z Calcd for $C_{17}H_{19}O_8N_2$ $[M-H]^-$ 379.1147. Found 379.1151.

(S)-1,3-Dihydroxy-3,7-dimethyloct-6-en-2-one (CPB Pheromone) (13a) To a solution of compound **12a** (591 mg, 1.56 mmol) in MeOH (16 mL) was added Et₂NH (85 μ L, 0.78 mmol) at r.t. After being stirred at r.t. for 10 min, the mixture was concentrated. The resulting residue was purified by flash CC (AcOEt–hexane, 1:2) to provide compound **13a** (274 mg, 95%) as a colorless oil. ¹H- and ¹³C-NMR data were identical with those reported.²²⁾ The enantiomeric purity was confirmed (97% ee) by chiral HPLC [CHIRALPAK ID 0.46×25 cm (Daicel), EtOH–hexane (15:85), 1.0 mL/min, 30°C, 210 nm (detect.); **13a**: 5.66 min, **13b**: 6.73 min]; $[\alpha]_D^{26}$ +3.6 ($c=1.00$, CHCl₃). IR (CHCl₃) cm^{-1} : 3607 and 3610 (OH), 1712 (CO). ¹H-NMR (300 MHz, CDCl₃) δ : 1.37 (3H, s, 3-CH₃), 1.58 and 1.67 (each 3H, s, *gem*-CH₃), 1.71 and 1.80 (each 1H,

ddd, $J=14, 9.5, 5.5$ Hz, 4-H₂), 1.84–2.16 (2H, m, 5-H₂), 2.97 (1H, s, OH), 2.97 (1H, t, $J=5$ Hz, OH), 4.46 and 4.53 (each 1H, d, $J=20, 5$ Hz, 1-H₂), 5.04 (1H, tsept, $J=7, 1$ Hz, 6-H). ¹³C-NMR (75 MHz, CDCl₃) δ : 17.66, 22.15, 25.63, 26.12, 39.92, 64.65, 78.46, 122.95, 133.31, 214.15. HR-MS (ESI) m/z Calcd for $C_{10}H_{18}O_3Na$ $[M+Na]^+$ 209.1148. Found 209.1147.

(R)-13b

In the same manner as described above, compound **11b** (683 mg, 1.80 mmol) was converted into (R)-**13b** (308 mg, 92%) as a colorless oil. The enantiomeric purity was confirmed (98% ee) by chiral HPLC: $[\alpha]_D^{27}$ –2.4 ($c=1.00$, CHCl₃). HR-MS (ESI) m/z Calcd for $C_{10}H_{18}O_3Na$ $[M+Na]^+$ 209.1148. Found 209.1149.

Conflict of Interest The authors declare no conflict of interest.

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