Note

Improved Synthesis of 14-Methyl-1-octadecene, the Sex Pheromone of the Peach Leafminer Moth

Yoshiaki MANABE, Jun-ichi MINAMIKAWA,
Jun-ichiro OTSUBO and Yoshio TAMAKI*Division of Process Research,
Tokushima Second Factory,
Otsuka Pharmaceutical Co., Ltd.,
Tokushima 771-01, Japan*National Institute of Agro-Environmental Sciences,
Yatabe, Tsukuba, Ibaraki 305, Japan

Received August 30, 1984

Recently, 14-methyl-1-octadecene **1** has been isolated and identified¹⁾ as the sex pheromone of the peach leafminer moth, *Lyonetia clerkella* LINNÉ, which is one of the most destructive pests in peach orchards in Japan. The results of a preliminary field trapping test showed that the

synthesized racemic **1** had almost the same attractiveness as the extracted compound at the same dose level.¹⁾ Therefore, establishment of the benefits in using a large amount of synthesized **1** can be expected to provide help to peach orchards. However, the previous synthesis of **1**¹⁾ was apparently unsatisfactory in overall yield and disadvantageous for this purpose.

We describe here a simple, improved and more efficient synthesis of **1** involving a cuprate-catalyzed Grignard coupling reaction as the key step. As shown in Fig. 1, commercially available 1,12-dodecanediol **2** and 2-methyl-1-hexanol **5** were chosen for the starting materials.

The diol **2** was effectively converted to the bromohydrin **3** by treating with hydrobromic acid. After protecting the hydroxy group of **3** with 2,3-dihydropyran, the resulting tetrahydropyranyl ether **4** was subjected to a coupling reaction with the Grignard reagent **7**, which had been derived from **5** via the bromide **6**. The coupling reaction would not proceed in the absence of a catalyst, but in the presence of dilithium tetrachlorocuprate,²⁾ the reaction was completed in 16 hr at room temperature.^{*1} After an acid treatment, the deprotected 14-methyl-1-octadecanol **8** was isolated in a 77% overall yield. The compound **8** was converted to the bromide **9** by treating with hydrobromic acid and then dehydrobromination of **9** with potassium *tert*-butoxide in dimethyl sulfoxide/benzene gave **1** in a 55% yield. The obtained **1** was completely identical with

FIG. 1.

*1 In this type of reaction, the sulfonate has been claimed to be superior to the halide.³⁾ Therefore, an alternative combination of **10** and **11** was also attempted, but the yield of **8** was poor.

the formerly synthesized **1**¹⁾ in IR, NMR, GC and mass spectra, which agree well with the structure for **1**. The overall yield of **1** from **2** was 26%, this being about 10 times higher than by the previous method.¹⁾

EXPERIMENTAL

All melting points and boiling points were uncorrected. IR spectra were recorded on a Hitachi 215 infrared spectrophotometer. 90 MHz NMR spectra were obtained on a Varian EM 390 instrument in CDCl₃ using tetramethylsilane as an internal standard. EI mass spectra were measured on a Finigan MAT 312 at 70 eV.

12-Bromo-1-dodecanol 3. Compound **3** was prepared from 1,12-dodecanediol **2** according to the reported method,⁴⁾ mp 30 ~ 31.5°C (lit.⁴⁾ mp 28 ~ 30°C).

2-(12-Bromododecyloxy)tetrahydropyran 4. 2,3-Dihydropyran (12 g) and **3** (33 g) were dissolved in hexane (100 ml). A small piece of *p*-toluenesulfonic acid was added to the solution. An exothermic reaction started within 20 min and the inner temperature rose to around 35°C. After this reaction (about 30 min), the mixture was washed with saturated sodium bicarbonate solution, dried over MgSO₄ and the solvent was evaporated to afford 45 g (quantitative) of **4** as a colorless oil, η_D^{25} 1.4750; MS (*m/z*): 349 (M⁺). This oil was used for the next reaction without further purification.

1-Bromo-2-methylhexane 6. Hydrobromic acid (48%, 300 ml) and **5** (100 g) were refluxed for 7 hr. After cooling, the oily layer was separated and then distilled under reduced pressure to yield 138 g (89%) of **6** as a colorless oil, bp₄₀ 90 ~ 92°C; η_D^{25} 1.4460 (lit.⁵⁾ bp₈ 75 ~ 76°C, η_D^{25} 1.4461).

14-Methyl-1-octadecanol 8. To a mixture of the Grignard reagent **7**, which had been prepared from **6** (9 g) and Mg (1.2 g) in THF (50 ml), **7** (3.5 g) and a 0.4 M THF solution of Li₂CuCl₄ (1 ml) were added in one portion under a nitrogen atmosphere. The solution was kept at room temperature for 16 hr and then quenched by adding hydrochloric acid (10 ml). The solvent was evaporated and to the residue, *p*-toluenesulfonic acid (3.0 g), MeOH (24 ml) and water (6 ml) were added. The mixture was refluxed for 1 hr and the solvent was evaporated. The

residue was extracted with CH₂Cl₂, dried over MgSO₄ and concentrated to give crude **8**, which was purified by silica gel column chromatography (eluted by CH₂Cl₂) to afford 2.2 g (77%) of pure **8** as a colorless oil, η_D^{25} 1.4466; MS (*m/z*): 284 (M⁺); NMR (CDCl₃+D₂O) δ : 0.85 (6H, m), 1.24 (31H, broad s), 3.55 (2H, t, *J* = 6 Hz).

1-Bromo-14-methyloctadecane 9. A mixture of **8** (11 g) and 48% hydrobromic acid (15 ml) was refluxed for 3 hr on an oil bath. The reaction mixture was cooled, extracted with hexane, dried over MgSO₄ and concentrated. The residue was purified by silica gel column chromatography (eluted by hexane) to yield 11 g (89%) of **9** as a colorless oil, η_D^{25} 1.4630; MS (*m/z*): 347 (M⁺); NMR δ : 0.87 (6H, m), 1.25 (31H, broad s), 3.33 (2H, t, *J* = 6 Hz).

14-Methyl-1-octadecene 1. A solution of **9** (11 g) in benzene (60 ml) and a 1.0 M DMSO solution of potassium *tert*-butoxide (60 ml) were mixed. Immediately, an exothermic reaction occurred and the temperature rose to 60 ~ 70°C. After 10 min, the mixture was acidified with dil. HCl and the upper layer was separated. The aqueous layer was extracted twice with hexane and the combined extracts were dried over MgSO₄. After the concentration, the residue was purified by silica gel column chromatography (eluted by hexane) and then distilled to afford 4.6 g (55%) of pure **1** as a colorless oil. bp_{0.5} 120 ~ 125°C; η_D^{25} 1.4430; MS (*m/z*): 266 (M⁺); NMR δ : 0.89 (6H, m), 1.26 (27H, broad s), 2.04 (2H, m), 4.93 (1H, ddt, *J* = 10 Hz, 2 Hz, *ca.* 1 Hz), 4.99 (1H, ddt, *J* = 17 Hz, 2 Hz, *ca.* 1 Hz), 5.81 (1H, m); IR (neat): 1640 cm⁻¹; Anal. Found: C, 86.26; H, 14.93. Calcd. for C₁₉H₃₈: C, 85.63; H, 14.38%.

Acknowledgment. We wish to thank Professor K. Mori of The University of Tokyo for his helpful discussions.

REFERENCES

- 1) H. Sugie, Y. Tamaki, R. Sato and M. Kumakura, *Appl. Entomol. and Zool.*, **19**, 323 (1984).
- 2) M. Tamura and J. Kochi, *Synthesis*, 303 (1971).
- 3) G. Fouquet and M. Schlosser, *Angew. Chem. Internat. Edit.*, **13**, 82 (1974).
- 4) G. Cerichelli, G. Illuminati and C. Lillocci, *J. Org. Chem.*, **45**, 3952 (1980).
- 5) B. J. Meakin, F. R. Mumford and E. R. Waed, *J. Pharm. Pharmacol.*, **11**, 540 (1959).