Dimethyl *cis*-5-oxo-2,3-pyrrolidinedicarboxylate (11a): colorless prisms [silica gel column chromatography with $CHCl_3$/EtOAc (2:1 v/v)]; mp 74.5–76.5 °C; IR (KBr) 3220, 1740, 1630, 1430, 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.57 (dd, J_{gem} = 16.9 Hz and J_{4-3} = 9.2 Hz, 1 H, one of H-4), 2.80 (dd, J_{gem} = 16.9 Hz and J_{4-3} = 8.4 Hz, 1 H, the other of H-4), 3.63 (dt, J_{3-4} = 9.2 and 8.4 Hz and J_{3-2} = 8.4 Hz, H-3), 3.72, 3.74 (each s, each 3 H, COOMe), 4.47 (d, J_{2-3} = 8.4 Hz, 1 H, 2-H), 7.48 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ 32.70 (C-4), 42.58 (C-3), 52.50, 52.60 (each COOMe), 57.28 (C-2), 170.61, 171.02 (each COOMe), 176.45 (C-5); MS *m/z* (rel intensity) 202 (M^+ + 1, 12), 201 (M^+, 9), 174 (32), 173 (22), 142 (81), 115 (12), 114 (base peak), 88 (42), 82 (22). Anal. Calcd for $C_8H_{11}NO_5$: C, 47.74; H, 5.51; N, 6.97. Found: C, 47.91; H, 5.53; N, 6.84.

Dimethyl *cis*-2-methyl-5-oxo-2,3-pyrrolidinedicarboxylate (11b): colorless prisms [silica gel column chromatography with $CHCl_3$/EtOAc (2:1 v/v)]; mp 110.5–112 °C; IR (KBr) 3160, 1720, 1690, 1200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68 (s, 3 H, Me), 2.59 (dd, J_{gem} = 17.2 Hz and J_{4-3} = 9.2 Hz, 1 H, one of H-4), 2.89 (dd, J_{gem} = 17.2 Hz and J_{4-3} = 9.5 Hz, 1 H, the other of H-4), 3.20 (dd, J_{3-4} = 9.5 Hz and 9.2 Hz, 1 H, H-3), 3.72 (s, 6 H, COOMe), 7.53 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ 24.66 (2-Me), 33.55 (C-4), 50.15 (C-3), 52.38, 52.80 (each COOMe), 64.22 (C-2), 170.89, 172.29 (each COOMe), 175.66 (C-5); MS *m/z* (rel intensity) 216 (M^+ + 1, 2), 215 (M^+, 1), 157 (8), 156 (base peak). Anal. Calcd for $C_9H_{13}NO_5$: C, 50.23; H, 6.09; N, 6.51. Found: C, 50.42; H, 6.18; N, 6.41.

A Novel Carbon–Carbon Bond-Forming Reaction of Triflates with Copper(I)-Catalyzed Grignard Reagents. A New Concise and Enantiospecific Synthesis of (+)-*exo*-Brevicomin, (5*R*,6*S*)-(−)-6-Acetoxy-5-hexadecanolide, and L-Factor[1]

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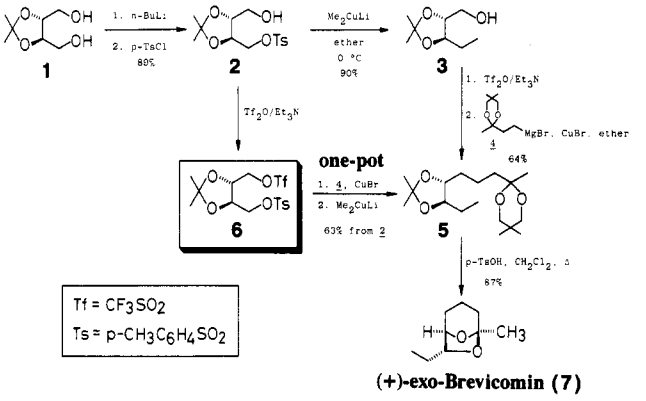
We describe here a full account of a highly concise and enantiospecific synthesis of (+)-*exo*-brevicomin (**7**), (5*R*,6*S*)-(−)-6-acetoxy-5-hexadecanolide (**11**), and L-factor (**16**) originating from D- or L-tartrates as chiral sources. The synthesis employs an efficient carbon–carbon bond-forming reaction of triflates with copper(I)-catalyzed Grignard reagents and, as a consequence, tosyl–triflate derivatives **6** and **15** were found to be a versatile intermediate. This methodology completed the synthetic scheme involving a five-step sequence from **1** to **7**, a 10-step sequence from **2** to **11**, and a seven-step sequence from **12** to **16**. The results present a new rapid means to derive optically active natural products from readily available chiral building blocks.

In recent years, a great deal of success has been achieved in the field of total synthesis of optically active natural products from readily available chiral building blocks.[2] In spite of these enormous advances for amplifying such a convenient chiral source, frequently it becomes a serious problem to elaborate the side chain on the carbon center bearing a β-oxygen functionality.[3,4] However, because of the electron-withdrawing nature of β-oxygen it is generally accepted that alkylation through nucleophilic displacement reaction is not so easy[5] except for the use of highly reactive nucleophiles such as organocuprate reagents.[6,7] To circumvent this difficulty, the usual method consists of alkylation on the epoxide intermediates (eq 1)[8] or oxidation to the corresponding aldehydes followed by Wittig-type olefination (eq 2).[9] More recently, as an alternative ap-

Scheme I



(1) The preliminary work was presented at the 1989 International Chemical Congress of Pacific Basin Societies, Honolulu, HI, December 17–22, 1989 (Abstract ORGN 0425).

(2) (a) Jurczak, J.; Pikul, S.; Bauer, T. *Tetrahedron* **1986**, *42*, 447. (b) Scott, J. W. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Ed.; Academic Press: New York, 1984; Vol. 4, pp 1–226. (c) Inch, T. D. *Tetrahedron* **1984**, *40*, 3161. (d) Hanessian, S. *Total Synthesis of Natural Products: The "Chiron" Approach*; Pergamon Press: Oxford, 1983. (e) Fraser-Reid, B.; Anderson, R. C. *Fortschr. Chem. Org. Naturst.* **1980**, *39*, 1.

(3) For example, see: (a) Overman, L. E.; Thompson, A. S. *J. Am. Chem. Soc.* **1988**, *110*, 2248. (b) Solladie, G.; Hutt, J. *Tetrahedron Lett.* **1987**, *28*, 797.

(4) The similar problem happens in the synthetic study of compactin. For a general treatment on this topic, see: Rosen, T.; Heathcock, C. H. *Tetrahedron* **1986**, *42*, 4909. See also: Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; da Silva, G. V. J.; Majewski, M.; Anderson, P. C.; Haugen, R. D.; Heerze, L. D. *J. Am. Chem. Soc.* **1988**, *110*, 6914. Kozikowski, A. P.; Li, C.-S. *J. Org. Chem.* **1987**, *52*, 3541. Keck, G. E.; Kachensky, D. F. *Ibid.* **1986**, *51*, 2487.

(5) Streitwieser, A. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962; pp 16–18.

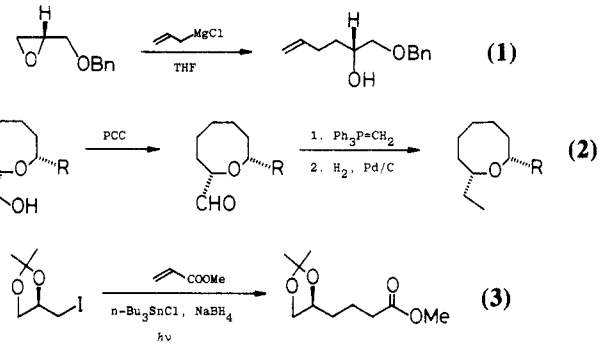
(6) For review, see: Lipshutz, B. H. *Synthesis* **1987**, 325. Erdik, E. *Tetrahedron* **1984**, *40*, 641. Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980. Posner, G. H. *Org. React.* **1975**, *22*, 253. See also: Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7777.

(7) Very limited success has been realized with the other carbon nucleophiles. For example, see: Lipshutz, B. H.; Moretti, R.; Crow, R. *Tetrahedron Lett.* **1989**, *30*, 15. Murai, A. *Pure Appl. Chem.* **1989**, *61*, 393. Murai, A.; Tanimoto, N.; Sakamoto, N.; Masamune, T. *J. Am. Chem. Soc.* **1988**, *110*, 1985. Grieco, P. A.; Lis, R.; Zelle, R. E.; Finn, J. *Ibid.* **1986**, *108*, 5908. Lipshutz, B. H.; Kotsuki, H.; Lew, W. *Tetrahedron Lett.* **1986**, *27*, 4825. Majewski, M.; Clive, D. L. J.; Anderson, P. C. *Ibid.* **1984**, *25*, 2101. Takano, S.; Goto, E.; Hirama, M.; Ogasawara, K. *Heterocycles* **1981**, *16*, 951.

(8) For example, see: Takano, S.; Moriya, M.; Iwabuchi, Y.; Ogasawara, K. *Tetrahedron Lett.* **1989**, *30*, 3805. Takano, S.; Ogasawara, K. *J. Syn. Org. Chem. Jpn.* **1989**, *47*, 813.

(9) For example, see: Carling, R. W.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1986**, 565.

0022-3263/90/1955-4417$02.50/0



proach, Giese has pointed out that the tin-mediated radical carbon–carbon coupling reaction is useful to achieve the desired reaction (eq 3).[10] Although such a protocol does not loose its own synthetic value, it suffers from the simplicity and general flexibility.

Recently, we have explored methods for the direct nucleophilic alkylation at the carbon center bearing a β-oxygen atom by taking advantage of the exceedingly reactive nature of trifluoromethanesulfonate (triflates).[11,12] Our method, notable for its simplicity, provides a highly practical route to derive chiral building blocks in good yields. Herein we describe a particularly short and highly elegant synthesis of some biologically active natural products by using this powerful carbon–carbon bond-forming reaction as the key step.

Results and Discussion

Synthesis of (+)-*exo*-Brevicomin.[13] (+)-*exo*-Brevicomin is known to be a key component of the aggregation pheromone of western pine beetle, a principal pest in North America,[14] and several synthetic studies have been developed to date.[15,16] Our route to a reasonable precursor, **5**, based on a straightforward carbon–carbon bond-constructing methodology from the enantiomerically pure diol **1**[17] is shown in Scheme I.

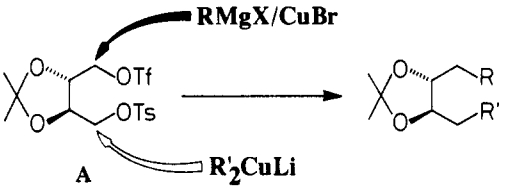


Figure 1. One-pot double alkylation strategy.

Treatment of diol **1** with 1.05 equiv of *n*-butyllithium followed by 1.0 equiv of *p*-toluenesulfonyl chloride gave monotosylate **2** in 89% yield.[18] Without protection of its free alcohol[19] subsequent alkylation with 6.0 equiv of Me_2CuLi led to alcohol **3** in 90% yield. After conversion of **3** to the corresponding triflate in a usual manner, exposure to our new alkylation technology by using the Grignard reagent **4**[20] in ether[21] containing a catalytic amount of CuBr provided the key intermediate **5**, $[\alpha]_D$ +16.8°, in 64% yield; the overall yield for this four-step sequence was 51.3%.

Although the established stepwise build-up technique above is sufficient to demonstrate the potential synthetic utility of copper(I)-catalyzed Grignard reactions on triflates, we further focused attention on the more concise approach.

Considering both the greater leaving property of triflates and the highly reactive nature of organocuprate reagents, it will be easy to carry out the required attachment of each fragment on the divergent molecule such as tosyl–triflate derivative A in one-pot operation (Figure 1). Thus, we expected that the first alkylation must occur predominantly on the triflate function when copper(I)-catalyzed Grignard reagents were added and, thereafter, addition of organocuprate reagents leads to a second alkylation on the tosylate function.[22]

Tosylate **2** was converted to tosyl–triflate **6**, $[\alpha]_D$ +7.6°, under the normal conditions in order to realize this expectation. Then one-pot double alkylation of **6** was accomplished first by reaction with 1.06 equiv of **4** in the presence of a catalytic amount of CuBr (0 °C for 4 h) followed by introduction of 3 equiv of Me_2CuLi (room temperature for 10 h) to afford **5** in 63% overall yield from **2**. As can be seen, ingenious and remarkable differences in reactivity between tosylate and triflate functions are particularly noteworthy: this simple procedure provides a new rapid means for reaching the final success.

The last step in completing the target molecule **7** was cleanly performed by treatment with a catalytic amount of *p*-toulenesulfonic acid in refluxing dichloromethane in 87% yield. The spectroscopic properties (^1H and ^{13}C

(10) Giese, B. *Radicals In Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986.

(11) Kotsuki, H.; Kadota, I.; Ochi, M. *Tetrahedron Lett.* **1989**, *30*, 1281.

(12) On the use of triflate for the similar purpose only very few precedents are appeared in the literature: Kennedy, R. M.; Abiko, A.; Takemasa, T.; Okamoto, H.; Masamune, S. *Tetrahedron Lett.* **1988**, *29*, 451. Imoto, M.; Kusumoto, S.; Shiba, T. *Ibid.* **1987**, *28*, 6235. Masamune, S.; Ma, P.; Okumoto, H.; Ellingboe, J. W.; Ito, Y. *J. Org. Chem.* **1984**, *49*, 2834. See also ref 3b.

(13) For the preliminary report of this work, see: Kotsuki, H.; Kadota, I.; Ochi, M. *Tetrahedron Lett.* **1989**, *30*, 3999.

(14) Wood, D. L.; Browne, L. E.; Ewing, B.; Lindahl, K.; Bedard, W. D.; Tilden, P. E.; Mori, K.; Pitman, G. B.; Hughes, P. R. *Science* **1976**, *192*, 896. Bellas, T. E.; Brownlee, R. G.; Silverstein, R. M. *Tetrahedron* **1969**, *25*, 5149. Silverstein, R. M.; Brownlee, R. G.; Bellas, T. E.; Wood, D. L.; Browne, L. E. *Science* **1968**, *159*, 889.

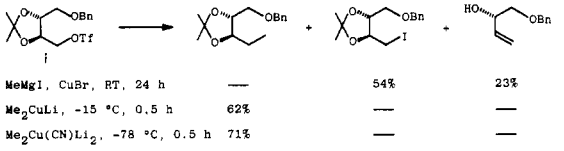
(15) For reviews, see: Mori, K. *Tetrahedron* **1989**, *45*, 3233. Mori, K. In *Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. 4, pp 1–183.

(16) For the recent work, see: (a) Chong, J. M.; Mar, E. K. *Tetrahedron* **1989**, *45*, 7709. (b) Ramaswamy, S.; Oehlschlager, A. C. *Can. J. Chem.* **1989**, *67*, 794. (c) Padwa, A.; Chinn, R. L.; Zhi, L. *Tetrahedron Lett.* **1989**, *30*, 1491. (d) Yadav, J. S.; Reddy, P. S.; Joshi, B. V. *Tetrahedron* **1988**, *44*, 7243. (e) Wershofen, S.; Scharf, H.-D. *Synthesis* **1988**, 854. (f) Giese, B.; Rupaner, R. *Ibid.* **1988**, 219. (g) Achmatowicz, B.; Wicha, J. *Liebigs Ann. Chem.* **1988**, 1135. (h) Singh, S. M.; Oehlschlager, A. C. *Can. J. Chem.* **1988**, *66*, 209. (i) Wilson, R. M.; Goudar, J. S.; Sidenstick, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 6895. (j) Ishibashi, H.; Uehara, C.; Komatsu, H.; Ikeda, M. *Chem. Pharm. Bull.* **1987**, *35*, 2750. (k) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412. (l) Oehlschlager, A. C.; Johnston, B. D. *Ibid.* **1987**, *52*, 940. (m) Seu, Y.-B.; Mori, K. *Agric. Biol. Chem.* **1986**, *50*, 2923. (n) Küfner, U.; Schmidt, R. R. *Synthesis* **1985**, 1060.

(17) Readily prepared from diethyl D-tartrate and now commercially available: Seebach, D. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Otto Salle Verlag: Frankfurt am Main, 1980; Vol. 2, pp 91–171. See also: Mash, E. A.; Nelson, K. A.; Van Deusen, S.; Hemperly, S. B. *Org. Synth.* **1989**, *68*, 92.

(18) The reported procedure using *p*-toluenesulfonyl chloride and pyridine to obtain **2** is less satisfactory (61% yield). See ref 17. See also: McDougal, P. G.; Rico, J. G.; Oh, Y.-I.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388.

(19) Cf. Meyer, H. H. *Liebigs Ann. Chem.* **1977**, 732. Unexpectedly, the use of benzyl ether protected triflate i gave very strange results.

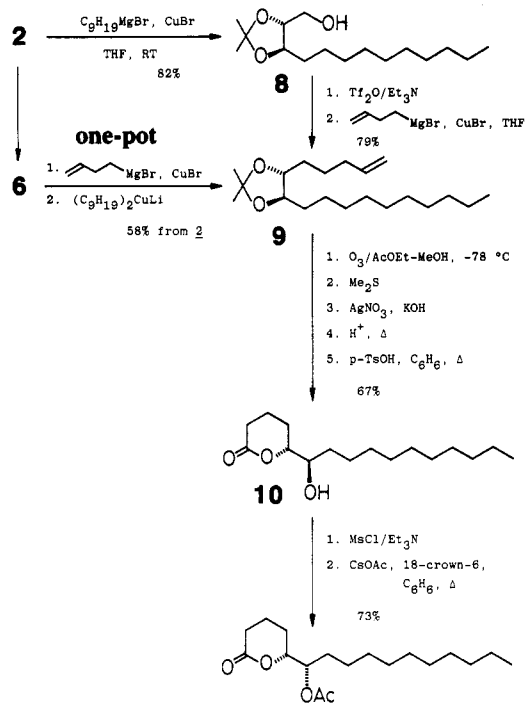


(20) Stowell, J. C.; Keith, D. R.; King, B. T. *Org. Synth.* **1983**, *62*, 140. See also: Stowell, J. C. *Chem. Rev.* **1984**, *84*, 409.

(21) The choice of solvent was important in this reaction and in THF no satisfactory result was obtained.

(22) Obviously, the reverse order of the addition of these two kinds of reagent will be unsuccessful owing to the indiscriminate attack of organocuprate reagents and the validity of this expectation was confirmed.

Scheme II



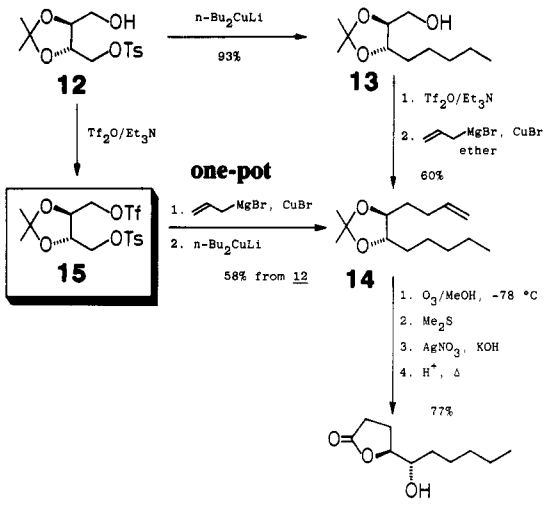
(5R,6S)-(-)-6-Acetoxy-5-hexadecanolide (11)

NMR, IR) of the product were identical with those reported for an authentic sample obtained from Prof. Masaki[23] and the optical rotation was determined as +61.7° (lit.[23] +81.6°).

Via tosyl–triflate **6** the overall yield of (+)-*exo*-brevicomin by the five-step sequence from diol **1** was extremely improved to 48.8%! Thus, among the several synthetic works on the title molecule, the present synthesis constitutes the highest total yield as well as the simplest route in an enantiomerically well-defined method.

Synthesis of (5*R*,6*S*)-(−)-6-Acetoxy-5-hexadecanolide. The successful strategy described above for deriving chiral building blocks via efficient carbon–carbon bond construction encouraged us to continue our study for the synthesis of (5*R*,6*S*)-(−)-6-acetoxy-5-hexadecanolide (**11**), the major component of the oviposition attractant pheromone from the apical droplet of eggs of the mosquito *Culex pipiens fatigans*.[24] Synthetically, this fascinating molecule offered a number of challenges, including asymmetric synthesis.[15,25,26]

Scheme III



L-Factor (16)

Our very intelligible strategy is shown in Scheme II in a similar manner as described in the preceding section utilizing monotosylate **2** as the same chiral source. Stepwise technology has started from the alkylation of **2** with 7.0 equiv of *n*-nonylmagensium bromide in the presence of 0.2 equiv of CuBr and alcohol **8** was isolated in 82% yield. After triflation of **8**, the action of 3-butenylmagnesium bromide/CuBr gave the key compound **9**, $[\alpha]_D$ +24.6°, in 79% yield.

On the other hand, the one-pot procedure from tosyl–triflate **6** through reaction first with 3-butenylmagnesium bromide/CuBr (0 °C, 1 h) and second with lithium di-*n*-nonylcuprate (−15 °C, 3 h) provided the same intermediate **9** in 58% overall yield from **2**.

Conversion of **9** to hydroxy δ-lactone **10**, $[\alpha]_D$ −11.0° (lit.[27] $[\alpha]_D$ −12.2°) was achieved in 67% overall yield by a simple one-pot operation for the following five-step sequence: (1) ozonolysis, (2) dimethyl sulfide reduction, (3) Ag_2O oxidation, (4) acidification to make free hydroxy acid, and (5) lactonization. The last step for introducing acetate function with accompanying configuration inversion was cleanly effected by applying Ikegami's procedure.[28] Thus, mesylation followed by treatment with 3 equiv of cesium acetate in the presence of 1.2 equiv of 18-crown-6 in refluxing benzene afforded the title molecule **11**, $[\alpha]_D$ −36.8° (lit.[26c] $[\alpha]_D$ −37.4°), in 73% yield. The complete inversion in this step was unambiguously confirmed by the measurements of 400-MHz ^1H NMR.

Starting from tosylate **2**, the overall yields of **11** for the 10-step sequence were 31.7% via **8** and 28.4% via **6**, respectively.

Synthesis of (4*S*,5*S*)-(+)-5-Hydroxy-4-decanolide (L-Factor). Extension of our synthetic methodology to the related naturally occurring hydroxy-γ-lactone **16**, isolated from *Streptomyces griseus* and so named as L-factor,[29] is shown in Scheme III. Despite the biological inactivity of this natural product, many synthetic efforts have been directed at devising an efficient strategy.[25,30]

(23) Masaki, Y.; Nagata, K.; Serizawa, Y.; Kaji, K. *Tetrahedron Lett.* **1982**, *23*, 5553.

(24) Otieno, W. A.; Onyango, T. O.; Pile, M. M.; Laurence, B. R.; Dawson, G. W.; Wadhams, L. J.; Pickett, J. A. *Bull. Entomol. Res.* **1988**, *78*, 463. Hwang, Y.-S.; Mulla, M. S.; Chaney, J. D.; Lin, G.-G.; Xu, H.-J. *J. Chem. Ecol.* **1987**, *13*, 245. Laurence, B. R.; Mori, K.; Otsuka, T.; Pickett, J. A.; Wadhams, L. J. *Ibid.* **1985**, *11*, 643. Laurence, B. R.; Pickett, J. A. *Bull Entomol. Res.* **1985**, *75*, 283; *J. Chem. Soc., Chem. Commun.* **1982**, 59.

(25) For a review see: Jefford, C. W.; Jaggi, D.; Sledeski, A. W.; Boukouvalas, J. *Stud. Nat. Prod. Chem.* **1989**, *3*, 157.

(26) For the recent work, see: (a) Ochiai, M.; Ukita, T.; Iwaki, S.; Nagao, Y.; Fujita, E. *J. Org. Chem.* **1989**, *54*, 4832. (b) Kawamura, F.; Tayano, T.; Satoh, Y.; Hara, S.; Suzuki, A. *Chem. Lett.* **1989**, 1723. (c) Kang, S.-K.; Cho, I.-H *Tetrahedron Lett.* **1989**, *30*, 743 and references cited therein. (d) Rahman, S. S.; Wakefield, B. J.; Roberts, S. M.; Dowle, M. D. *J. Chem. Soc., Chem. Commun.* **1989**, 303. (e) Ichimoto, I.; Yoshizawa, T.; Machiya, K.; Kirihata, M.; Ueda, H. *Chem. Express* **1988**, *3*, 687. (f) Prasit, P.; Rokach, J. *J. Org. Chem.* **1988**, *53*, 4422. (g) Sala, L. F.; Cravero, R. M.; Signorella, S. R.; González-Sierra, M.; Rúveda, E. A. *Syn. Commun.* **1987**, *17*, 1287. (h) Kamikawa, T.; Yamagiwa, Y.; Katsui, T. *Kinki Daigaku Rikogakubu Kenkyu Hokoku* **1987**, 79.

(27) Machiya, K.; Ichimoto, I.; Kirihara, M.; Ueda, H. *Agric. Biol. Chem.* **1985**, *49*, 643.

(28) Torisawa, Y.; Okabe, H.; Ikegami, S. *Chem. Lett.* **1984**, 1555.

(29) Gräfe, U.; Eritt, I. *J. Antibiot.* **1983**, *36*, 1592. Gräfe, U.; Reinhardt, G.; Schade, W.; Krebs, D.; Eritt, I.; Fleck, W. F.; Heinrich, H.; Radics, L. *Ibid.* **1982**, *35*, 609.

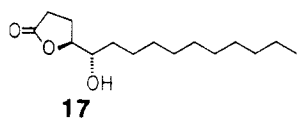
Similarly, as described above, the obvious route is the use of monotosylate **12**,[17] an enantiomer of **2**, as a chiral starting material. According to the literature method,[31] **12** was alkylated with lithium di-*n*-butylcuprate to afford **13** in rather improved yield (93%). Then the reaction of CuBr-catalyzed allylmagnesium bromide with the triflate derivative of **13** in ether[21] gave **14** in 60% yield. On the other hand, via tosyl–triflate **15**, one-pot double alkylation employing allylmagnesium bromide/CuBr and lithium di-*n*-butylcuprate furnished **14** in 58% overall yield from **12**. Finally, transformation of **14** to the target hydroxy-γ-lactone **16**, $[\alpha]_D$ +31.2° (lit.[30j] $[\alpha]_D$ +33.2°), was effected in a similar manner to that shown in Scheme II in 77% yield.

In this case the overall yield of **16** for the seven-step procedure was 43.0% via **13** and 44.7% via **15**, respectively.

Conclusion

The investigations recorded here introduce a highly concise and efficient procedure as illustrated by the enantiospecific synthesis of (+)-*exo*-brevicomin, (5*R*,6*S*)-(−)-6-acetoxy-5-hexadecanolide, and L-factor originating from D- or L-tartrate as chiral sources. In this strategy the potentially valuable and intriguing intermediates of tosyl–triflates **6** and **15** have been employed as a key component. Of general utility are the methods described here for efficient carbon–carbon bond homologation via triflates and for ease in production of the target molecules with the correct absolute and relative stereochemistry. In addition, because of the ready availability of starting chiral diol in both enantiomers,[17] the strategy described here permits the preparation of either antipode of natural products.

Furthermore, the successful results shown in Schemes II and III indicate that the procedure is generally applicable for other optically active hydroxy lactones, and hence **17**, an important intermediate to disparlure,[32] should be also easily accessible.



17 ⟹ **(+)-Disparlure**

Experimental Section

General Methods. All melting points are uncorrected. The NMR spectra were recorded on a Hitachi R-90H spectrometer (90 MHz for ^1H NMR analysis and 22.6 MHz for ^{13}C NMR analysis) or on a JEOL GX-400 spectrometer (400 MHz for ^1H NMR analysis). All NMR spectra were taken in $CDCl_3$ solutions and are reported in parts per million (δ) downfield from TMS, which was used as an internal standard. The IR spectra (cm^{-1}) were measured with a JASCO Model A-302 infrared spectrophotometer. High-resolution mass spectra were obtained with a JEOL HX-100 spectrometer. Optical rotations were measured on a Union PM-101 polarimeter. Thin-layer chromatography (TLC) was conducted by using Merck precoated kieselgel 60F-254 plates (0.25 mm). Preparative TLC was carried out on 2-mm-thick Merck kieselgel 60PF-254 and column chromatography was done on Wakogel C-300.

All solvents were dried immediately before use. Ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone ketyl; dichloromethane, triethylamine, dimethyl sulfide, and dimethyl sulfoxide (DMSO) were distilled from CaH_2; MeOH was distilled from magnesium methoxide. All reactions involving air- and/or moisture-sensitive materials were carried out under an argon atmosphere. All extracts were dried over Na_2SO_4.

(4*R*,5*R*)-[5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl *p*-Toluenesulfonate (2). To a solution of **1** (100 mg, 0.62 mmol) in THF (2 mL) and DMSO (0.5 mL) at −15 °C was added *n*-BuLi (1.58 M in hexane; 0.41 mL, 0.65 mmol), and the reaction mixture was stirred at room temperature for 15 min. Then to the resulting solution at 0 °C was introduced *p*-toluenesulfonyl chloride (120 mg, 0.62 mmol) in THF (1 mL), and the reaction mixture was stirred at room temperature for 1 h. After being quenched with water followed by evaporation of most of the organic solvent, the residue was poured into ether and rinsed with saturated NaCl. Following solvent removal, the crude product was purified by preparative TLC to give 175 mg(89%) of **2** as a colorless oil: R_f 0.42 (ether); $[\alpha]^{21}_D$ +11.3° (*c* 2.70, $CHCl_3$) [lit.[17] $[\alpha]^{25}_D$ −12.2° (*c* 21.82, $CHCl_3$) for the enantiomer].

(4*R*,5*R*)-4-Ethyl-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (3). To a solution of Me_2CuLi, prepared from CuI (370 mg, 1.92 mmol) and MeLi (1.56 M in ether; 2.5 mL, 3.84 mmol), in ether (2 mL) at −30 °C was added an ether (3 mL) solution of monotosylate **2** (100 mg, 0.32 mmol), and the reaction mixture was slowly warmed to 0 °C. After 3 h of stirring, the mixture was quenched with saturated NH_4Cl–aqueous NH_3 (9:1) and extracted with ether. Following solvent removal, the crude product was purified by column chromatography (hexane/ether, 1:1) to give 46 mg (90%) of **3** as a colorless oil: R_f 0.24 (hexane/ether, 1:1); $[\alpha]^{20}_D$ +18.7° (*c* 1.88, $CHCl_3$) [lit.[16d] $[\alpha]_D$ −21.2° (*c* 5, $CHCl_3$) for the enantiomer].

(4*R*,5*R*)-5-Ethyl-4-[3-(2,5,5-trimethyl-1,3-dioxan-2-yl)-propyl]-2,2-dimethyl-1,3-dioxolane (5). To a mixture of **3** (300 mg, 1.88 mmol) and triethylamine (780 μL) in CH_2Cl_2 (10 mL) at −15 °C was added dropwise triflic anhydride (480 μL, 2.8 mmol) in CH_2Cl_2 (3 mL), and the reaction mixture was stirred for 0.5 h. After dilution with CH_2Cl_2, the organic layer was rinsed with water, saturated $NaHCO_3$, and saturated NaCl. The extract was dried over Na_2SO_4 and *filtered through a silica gel pad*.[33] Following solvent removal, the crude triflate was azeotropically dried with toluene and used for the next reaction.

To a suspension of CuBr (54 mg, 0.4 mmol) in ether (10 mL) at 0 °C was added the Grignard reagent **4** (0.5 M in THF; 5.6 mL, 2.8 mmol)[20] followed by the above-obtained triflate in ether (5 mL), and the reaction mixture was stirred for 3.5 h.[34] After being quenched with saturated NH_4Cl/aqueous NH_3 (9:1), the mixture was filtered through Celite and the filtrate was rinsed with saturated $NaHCO_3$ and saturated NaCl. Following solvent removal, the crude product was purified by column chromatography (hexane/ether, 4:1) to give 361 mg (64%) of **5** as a colorless oil: R_f 0.27 (hexane/ether, 4:1); $[\alpha]^{17}_D$ +16.8° (*c* 0.80, $CHCl_3$); IR (neat) 2970, 2930, 2920, 2850, 1460, 1390, 1370, 1360, 1250, 1230, 1200, 1100, 860, 730; ^1H NMR 0.88 (3 H, s), 0.99 (3 H, t, *J* = 6.9 Hz), 1.03 (3 H, s), 1.37 (9 H, s), 1.4–1.8 (8 H, m), 3.4–3.7 (6 H, m); ^{13}C NMR 10.29, 20.08, 20.23, 22.58, 22.91, 25.84, 27.36, 27.42, 30.05, 33.40, 38.55, 70.38, 80.57, 82.12, 98.92, 107.70; HRMS calcd for $C_{17}H_{32}O_4$ 300.2301, found 300.2303.

(4*R*,5*R*)-[5-[(*p*-Tolylsulfonyl)oxy]-2,2-dimethyl-1,3-dioxolan-4-yl]methyl Triflate (6). To a solution of **2** (165 mg, 0.52 mmol) and triethylamine (170 μL) in CH_2Cl_2 (3 mL) at −15 °C was added dropwise triflic anhydride (130 μL, 0.78 mmol) in

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(31) Suemune, H.; Harabe, T.; Sakai, K. *Chem. Pharm. Bull.* **1988**, *36*, 3632.

(32) Kametani, T.; Tsubuki, M.; Honda, T. *Chem. Pharm. Bull.* **1988**, *36*, 3706. Iwaki, S.; Marumo, S.; Saito, T.; Yamada, M.; Katagiri, K. *J. Am. Chem. Soc.* **1974**, *96*, 7842.

(33) This technique is very convenient to remove any polar impurity, which caused a rather decreased yield for the subsequent coupling reactions.

(34) Usually at the end of this type of coupling reaction a considerable amount of black deposit was formed.

CH_2Cl_2 (1 mL), and the reaction mixture was stirred for 20 min. Usual workup gave the crude tosyl–triflate **6**, which was azeotropically dried with toluene and used in the next reaction.

A spectroscopically homogeneous sample was prepared by purification through a short silica gel column: R_f 0.43 (hexane/ether, 1:1); $[\alpha]^{21}_D$ +7.6° (*c* 1.26, $CHCl_3$); IR (neat) 3000, 2950, 1600, 1420, 1370, 1250, 1210, 1190, 1180, 1150, 1100, 990, 950, 815, 785, 760, 660, 610, 550; ^{1}H NMR 1.37 (3 H, s), 1.39 (3 H, s), 2.46 (3 H, s), 4.14 (4 H, m), 4.56 (2 H, m), 7.36 (2 H, d, J = 8.4 Hz), 7.80 (2 H, d, J = 8.4 Hz).

One-Pot Preparation of 5 from 6. To a suspension of CuBr (15 mg, 0.1 mmol) in ether (2 mL) at 0 °C was added the Grignard reagent **4** (1.1 mL, 0.55 mmol), followed by the above-obtained tosyl–triflate **6** in ether (3 mL), and the reaction mixture was stirred at the same temperature for 4 h. Then 3 equiv of Me_2CuLi in ether (3 mL) was introduced and the reaction mixture was stirred at room temperature for 10 h. Usual workup followed by column chromatography gave 98 mg (63%) of **5**.

Preparation of (+)-*exo*-Brevicomin (7). A solution of **5** (380 mg, 1.27 mmol) containing a catalytic amount of *p*-toluenesulfonic acid in CH_2Cl_2 (15 mL) was refluxed for 2 h. The organic layer was rinsed with saturated $NaHCO_3$ and saturated NaCl. Following solvent removal, the crude product was purified by column chromatography to give 173 mg (87%) of **7** as a colorless oil: R_f 0.32 (pentane/ether, 10:1); $[\alpha]^{21}_D$ +67.6° (*c* 1.0, ether) [lit.[23] $[\alpha]_D$ +81.6° (ether)]; IR (neat) 2950, 1460, 1380, 1235, 1030, 1000, 845; ^{1}H NMR 0.91 (3 H, t, J = 6.8 Hz), 1.42 (3 H, s), 1.3–1.9 (8 H, m), 3.93 (1 H, t, J = 6.2 Hz), 4.12 (1 H, br); ^{13}C NMR 9.80, 17.27, 25.08, 28.03, 28.61, 35.02, 78.25, 81.12, 107.61; HRMS calcd for $C_9H_{16}O_2$ 156.1150, found 156.1160.

(4*R*,5*R*)-4-Decyl-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (8). To a suspension of CuBr (260 mg, 1.8 mmol) in THF (10 mL) at 0 °C was added $C_9H_{19}MgBr$ (0.67 M in ether; 13 mL, 8.6 mmol), followed by monotosylate **2** (390 mg, 1.23 mmol) in THF (5 mL), and the reaction mixture was stirred at room temperature for 5 h. After being quenched with saturated NH_4Cl/aqueous NH_3 (9:1), the insoluble substance was removed by filtration through Celite. The filtrate was concentrated and the residue was poured into ether. The organic layer was rinsed with water and saturated NaCl. Following solvent removal, the crude product was purified by column chromatography to give 273 mg (82%) of **8** as a colorless oil: R_f 0.31 (hexane/ether, 2:1); $[\alpha]^{24}_D$ +21.1° (*c* 1.52, $CHCl_3$); IR (neat) 3350, 2920, 2850, 1460, 1375, 1240, 1210, 1100, 1050; ^{1}H NMR 0.88 (3 H, t, J = 6.5 Hz), 1.26 (14 H, s), 1.40 (6 H, s), 1.3–1.7 (4 H, m), 2.00 (1 H, br), 3.3–3.9 (4 H, m); ^{13}C NMR 13.92, 22.55, 25.84, 26.91, 27.21, 29.19, 29.37, 29.47 (×2), 29.59, 31.75, 33.06, 62.09, 77.00, 81.54, 108.31; HRMS calcd for $C_{16}H_{32}O_3 - CH_3$ 257.2117, found 257.2130.

(4*R*,5*R*)-5-Decyl-2,2-dimethyl-4-(1-penten-5-yl)-1,3-dioxolane (9). Via the procedure described for **3** → **5**, alcohol **8** (310 mg, 1.14 mmol) was triflated.

To a suspension of CuBr (35 mg, 0.2 mmol) in THF (3 mL) at 0 °C was added 3-butenylmagnesium bromide (0.69 M in ether; 2.5 mL, 1.7 mmol), followed by the above-obtained triflate in THF (5 mL), and the reaction mixture was stirred at the same temperature for 3 h. Usual workup followed by column chromatography gave 280 mg (79%) of **9** as a colorless oil: R_f 0.33 (hexane/ether, 20:1); $[\alpha]^{22}_D$ +24.6° (*c* 1.78 $CHCl_3$); IR (neat) 2920, 2850, 1640, 1450, 1375, 1365, 1235, 1100, 990, 910; ^{1}H NMR 0.88 (3 H, t, J = 6.5 Hz), 1.26 (14 H, s), 1.37 (6 H, s), 1.4–1.7 (8 H, m), 1.9–2.2 (2 H, m), 3.59 (2 H, m), 4.94 (1 H, m), 4.99 (1 H, m), 5.81 (1 H, ddt, J = 17.1, 9.7, 6.5 Hz); ^{13}C NMR 14.13, 22.73, 25.44, 26.17, 27.39 (×2), 29.37, 29.59, 29.65(×2), 29.83, 31.97, 32.45, 33.09, 33.80, 80.84, 80.99, 107.73, 114.62, 138.41; HRMS calcd for $C_{20}H_{38}O_2$ 310.2872, found 310.2859.

One-Pot Preparation of 9 from 6. Via the procedure described for **6** → **5**, 3-butenylmagnesium bromide (0.78 mL, 0.54 mmol) was added to a suspension of CuBr (14 mg, 0.1 mmol) in THF (2 mL) at 0 °C, followed by tosyl–triflate **6**, prepared from **2** (160 mg, 0.51 mmol), in THF (3 mL), and the reaction mixture was stirred at the same temperature for 1 h. Then $(C_9H_{19})_2CuLi$, prepared from CuI (495 mg, 2.6 mmol) and $C_9H_{19}Li$ (0.82 M in ether; 6.3 mL, 5.2 mmol) in dimethyl sulfide (3 mL), was introduced at −15 °C and the reaction mixture was allowed to stir for 3 h. Usual workup followed by column chromatography gave 91 mg (58%) of **9**.

(5*R*,6*R*)-6-Hydroxy-5-hexadecanolide (10). Through a solution of **9** (200 mg, 0.65 mmol) in 10 mL of MeOH–AcOEt (4:1) cooled in a dry ice–acetone bath was passed a slightly excess of ozone. To the resulting pale blue solution was added dimethyl sulfide (3 mL), and the reaction mixture was stirred for 0.5 h.

After evaporation of most of the solvent, the crude aldehyde was dissolved in MeOH (10 mL) and treated with $AgNO_3$ (340 mg, 2.0 mmol) in H_2O (1 mL) and KOH (225 mg, 4.0 mmol) in H_2O (1 mL) at 0 °C. After being stirred for 1 h, the mixture was acidified with concentrated HCl and gently refluxed for 0.5 h. Removal of the insoluble substance by filtration through Celite followed by extraction with AcOEt gave a crude hydroxy acid, which was treated with a small amount of *p*-toluenesulfonic acid in refluxing C_6H_6 (10 mL) for 1 h. The mixture was diluted with AcOEt and rinsed with saturated $NaHCO_3$ and saturated NaCl. Following solvent removal, the crude product was purified by column chromatography to give 118 mg (67%) of **10** as colorless plates: mp 73–74 °C (lit.[27] mp 67–69 °C); R_f 0.26 (hexane/AcOEt, 1:1); $[\alpha]^{23}_D$ −11.0° (*c* 0.9, $CHCl_3$) [lit.[27] $[\alpha]^{29}_D$ −12.2° (*c* 1.4, $CHCl_3$)]; IR ($CHCl_3$) 3400, 2910, 2850, 1720, 1460, 1240, 1160, 1050, 930; ^{1}H NMR 0.88 (3 H, t, J = 6.5 Hz), 1.26 (16 H, s), 1.4–1.7 (2 H, m), 1.7–2.2 (5 H, m), 2.4–2.7 (2 H, m), 3.52 (1 H, m), 4.13 (1 H, m); ^{13}C NMR 14.10, 18.49, 22.70, 24.25, 25.47, 29.31, 29.59 (×4), 29.68, 31.91, 32.76, 73.37, 83.13, 171.15; HRMS calcd for $C_{16}H_{30}O_3$ − H 269.2117, found 269.2135.

For the stereochemical assistance, **10** was converted to the corresponding acetate under standard conditions: ^{1}H NMR (400 MHz) 0.88 (3 H, t, J = 6.8 Hz), 1.26 (16 H, s), 1.55–2.00 (6 H, m), 2.09 (3 H, s), 2.44 (1 H, ddd, J = 17.7, 8.9, 7.3 Hz), 2.60 (1 H, ddd, J = 17.7, 6.4, 5.2 Hz), 4.35 (1 H, dt, J = 11.3, 3.7 Hz), 4.98 (1 H, ddd, J = 7.3, 6.7, 3.7 Hz).

Preparation of (5*R*,6*S*)-(−)-6-Acetoxy-5-hexadecanolide (11). To a solution of **10** (50 mg, 0.19 mmol) in CH_2Cl_2 (5 mL) at 0 °C were added triethylamine (56 μL, 0.4 mmol), methanesulfonyl chloride (18 μL, 0.23 mmol), and a catalytic amount of 4-(dimethylamino)pyridine, and the reaction mixture was stirred at room temperature for 0.5 h. Usual workup gave a crude mesylate.

A mixture of this mesylate, CsOAc (64 mg, 0.57 mmol), and 18-crown-6 (60 mg, 0.23 mmol) in C_6H_6 (5 mL) was refluxed for 21 h. The mixture was poured into ether and rinsed with water, saturated $NaHCO_3$, and saturated NaCl. Following solvent removal, the crude product was purified by column chromatography to give 43 mg (73%) of **11** as a colorless oil: R_f 0.24 (hexane/AcOEt, 2:1); $[\alpha]^{24}_D$ −36.8° (*c* 1.0, $CHCl_3$) [lit.[26c] $[\alpha]^{26}_D$ −37.4° (*c* 1.55, $CHCl_3$)]; IR (neat) 2930, 2860, 1740, 1460, 1370, 1230, 1060, 930; ^{1}H NMR (400 MHz) 0.88 (3 H, t, J = 6.8 Hz), 1.26 (16 H, s), 1.57–2.00 (6 H, m), 2.07 (3 H, s), 2.44 (1 H, ddd, J = 17.7, 7.2, 6.7 Hz), 2.59 (1 H, dt, J = 17.7, 6.5 Hz), 4.34 (1 H, ddd, J = 10.8, 5.1, 3.4 Hz), 4.98 (1 H, dt, J = 7.0, 5.1 Hz); ^{13}C NMR 14.13, 18.34, 21.05, 22.73, 23.61, 25.32, 29.34, 29.50 (×2), 29.62 (×4), 31.94, 74.35, 80.48, 170.30, 170.63; HRMS calcd for $C_{18}H_{32}O_4$ −H 311.2222, found 311.2216.

(4*S*,5*S*)-2,2-Dimethyl-4-(hydroxymethyl)-5-pentyl-1,3-dioxolane (13). According to the literature method,[31] monotosylate **12** (150 mg, 0.47 mmol) was reacted with 6 equiv of n-Bu_2CuLi to afford 88 mg (93%) of **13**.

(4*S*,5*S*)-4-(3-Buten-1-yl)-2,2-dimethyl-5-pentyl-1,3-dioxolane (14). Via the procedure described for **3** → **5**, **13** (130 mg, 0.64 mmol) was triflated with 1.5 equiv of triflic anhydride.

To a suspension of CuBr (20 mg, 0.13 mmol) in ether (1 mL) at 0 °C was added allylmagnesium bromide (0.22 M in ether; 4.4 mL, 0.96 mmol), followed by the above-obtained triflate in ether (3 mL), and the reaction mixture was stirred at room temperature for 15 h. Usual workup followed by column chromatography gave 87 mg (60%) of **14** as a colorless oil: R_f 0.49 (hexane/ether, 10:1); $[\alpha]^{21}_D$ −31.7° (*c* 1.32, $CHCl_3$); IR (neat) 2930, 1640, 1375, 1365, 1240, 1110, 990, 910, 875; ^{1}H NMR 0.89 (3 H, t, J = 6.5 Hz), 1.37 (6 H, s), 1.1–1.8 (10 H, m), 2.0–2.4 (2 H, m), 3.60 (2 H, m), 4.98 (1 H, m), 5.02 (1 H, m), 5.85 (1 H, ddt, J = 17.4, 9.9, 6.3 Hz); ^{13}C NMR 14.04, 22.61, 25.84, 27.39 (×2), 30.26, 32.03, 32.33, 33.00, 80.32, 80.90, 107.79, 114.72, 138.04; HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, found 226.1923.

One-Pot Preparation of 14 from 12. Via the procedure described for **2** → **6**, monotosylate **12** (150 mg, 0.47 mmol) was converted to the corresponding tosyl–triflate **15**: $[\alpha]^{22}_D$ −8.0° (*c*

1.08, $CHCl_3$).

To a suspension of CuBr (13 mg, 0.1 mmol) in ether (1 mL) at 0 °C was added allylmagnesium bromide (2.2 mL, 0.48 mmol), followed by the above-obtained tosyl-triflate **15** in ether (3 mL), and the reaction mixture was stirred at the same temperature for 3.5 h. Then n-Bu_2CuLi (1.4 mmol) in ether (3 mL) was introduced and the mixture was stirred at room temperature for 12 h. Usual workup followed by column chromatography gave 62 mg (58%) of **14**.

Preparation of L-Factor [(4*S*,5*S*)-(+)-5-Hydroxy-4-decanolide] (16). Through a solution of **14** (130 mg, 0.58 mmol) in 5 mL of MeOH cooled in a dry ice-acetone bath was passed a slightly excess of ozone. To the resulting pale blue solution was added dimethyl sulfide (1 mL), and the reaction mixture was slowly warmed to room temperature.

After evaporation of most of the solvent, the obtained crude aldehyde was dissolved in MeOH (5 mL) and treated with $AgNO_3$ (200 mg, 1.2 mmol) in H_2O (3 mL) and KOH (140 mg, 2.4 mmol) in H_2O (2 mL) at 0 °C for 0.5 h. At the end of the reaction the mixture was acidified with concentrated HCl and gently refluxed for 0.5 h. After removal of the insoluble substance by filtration through Celite, the filtrate was concentrated. The residue was poured into AcOEt and rinsed with saturated NaCl. Following solvent removal, the crude product was purified by column chromatography to give 83 mg (77%) of **16** as a colorless oil, which was crystallized in a refrigerator: mp 39–41 °C (lit.[30j] mp 42–44 °C); R_f 0.32 (ether); $[\alpha]^{20}_D$ +31.2° (c 0.96, $CHCl_3$) [lit.[30j] $[\alpha]^{21}_D$ +33.2° (c 1.11, $CHCl_3$)]; IR (neat) 3430, 2920, 2850, 1765, 1190, 780, 755; ^1H NMR 0.90 (3 H, t, J = 6.0 Hz), 1.2–1.8 (8 H, m), 1.9–2.7 (5 H, m), 3.3–3.7 (1 H, m), 4.42 (1 H, dt, J = 7.3, 4.4 Hz); ^{13}C NMR 13.89, 22.42, 23.95, 25.08, 28.58, 31.60, 32.85, 73.28, 82.92, 177.40; HRMS calcd for $C_{10}H_{18}O_3$ 186.1256, found 186.1263.

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Supplementary Material Available: Experimental data for **5**, **6**, **8–10**, and **14** (3 pages). Ordering information is given on any current masthead page.

Structure and Absolute Stereochemistry of the Epoxyquinol LL-C10037α and Related Metabolites from *Streptomyces* LL-C10037

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The structure of antibiotic LL-C10037α, produced by *Streptomyces* LL-C10037, was revised to the epoxyquinol **2** on the basis of a single-crystal X-ray diffraction analysis. Two other metabolites were isolated and characterized as 2-acetamido-4,5-dihydroxycyclohexenone and 2-acetamido-4-hydroxycyclohexenone. From application of the empirical "inverse quadrant rule" of Snatzke for epoxyquinols to the circular dichroism spectrum of **2**, the stereochemistry was inferred to be 4*S*,5*S*,6*S*. Preferring to rely on a non-empirical approach, the circular dichroism (CD) exciton chirality and X-ray crystallographic analyses of suitable derivatives were investigated to provide nonempirical approaches to establishing the absolute stereochemistry. Thus the 4-*p*-bromobenzoate of **2** was prepared, and the exciton chirality rules for interaction of the transition moments of the enone and benzoate chromophores were applied to the circular dichroism spectrum of this derivative, and a single-crystal X-ray diffraction analysis was carried out on the carbamate of **2** obtained with (*S*)-α-methylbenzylisocyanate. The exciton chirality analysis yielded 4*S* stereochemistry; thus, C-5 and C-6 also have the *S* configuration from the cis relationship established from the ^1H NMR spectrum. This absolute stereochemistry was also obtained from the X-ray diffraction analysis. The 4-*p*-bromobenzoates of **8** and **9** were also prepared, and exciton chirality analysis again indicated the 4*S* configuration for each.

Introduction

The antitumor metabolite LL-C10037α was isolated from *Streptomyces* LL-C10037 by researchers at Lederle Laboratories, and its gross structure was reported as **1**.[1] This structure represented the first reported occurrence of a γ-aminoepoxysemiquinone, and we wanted to explore its bioorganic implications.[2] As the initial part of our effort we repeated the spectral analysis with an authentic sample of LL-C10037α in order to confirm the structural assignment made earlier and to determine the relative configuration. In this paper data are presented for revising the structure of LL-C10037α, for establishing the structures of two additional metabolites produced by the same organism, and for defining the absolute stereochemistry of each metabolite.

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(2) Initial biosynthesis results have already been reported: Gould, S. J.; Shen, B.; Whittle, Y. G. *J. Am. Chem. Soc.* **1989**, *111*, 7932.

Table I

H	^1H NMR (400 MHz, DMSO-d_6) δ	^1H NMR (400 MHz, DMSO-d_6) multiplicity, J, Hz	^{13}C NMR (100.6 MHz, DMSO-d_6) δ
1			189.6
2			128.3
3	7.04	dd, J = 2.5, 2.7	128.3
4	4.79	ddd, J = 2.7, 3.1, 6.4	63.3
5	3.77	ddd, J = 2.5, 3.1, 4.2	53.7
6	3.55	d, J = 4.2	52.2
1′			169.5
2′ (CH_3)	2.04	s	23.7
OH	5.79	d, J = 6.4	
NH	9.04	br s	

Results and Discussion

Relative Stereochemistry of 2. The ^1H NMR data acquired by us for LL-C10037α were identical to that reported in the literature[1] (Table I). The only difference was in the interpretation of the chemical shifts of the two

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