CHEMISTRY LETTERS, pp. 1687-1688, 1985.

TOTAL SYNTHESIS OF (±)-(Z)-9-(BROMOMETHYLENE)-1,5,5-TRIMETHYLSPIRO[5.5]UNDECA-1,7-DIEN-3-ONE, A BROMINATED SESQUITERPENE OF CHAMIGRANE TYPE

Haruki NIWA, Yoshifumi YOSHIDA, Takashi HASEGAWA, and Kiyoyuki YAMADA<sup>\*</sup> Department of Chemistry, Faculty of Science, Nagoya University, Chikusa, Nagoya 464

The first total synthesis of  $(\pm)-(Z)-9-(bromomethylene)-1,5,5-$ trimethylspiro[5.5]undeca-1,7-dien-3-one, a chamigrane sesquiterpene having a novel bromomethylene group is described.

A number of halogenated sesquiterpenes of chamigrane type have been isolated from the red algae of the genus Laurencia.<sup>1)</sup> Nevertheless, the synthetic studies on these halogenated sesquiterpenes are very limited and only 10-bromo- $\alpha$ -chamigrene has so far been synthesized.<sup>2)</sup> In this communication, we wish to report a total synthesis of another brominated sesquiterpene of chamigrane type, (Z)-9-(bromomethylene)-1,5,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (<u>1</u>) isolated from Laurencia majuscula HARVEY by Suzuki and Kurosawa,<sup>3)</sup> in racemic form.



One of the key steps in the present synthesis is a spiroannelation of a cyclohexenone aldehyde 2 into the spiro[5.5] undecenone derivative 3.<sup>4)</sup> The preparation of 2 started from anisole. The Friedel-Crafts reaction<sup>5)</sup> of anisole with 5-methyl-1,5-hexanediol<sup>6,7)</sup> (AlCl<sub>3</sub>, 0 °C for 3 h and then room temp for 20 h) gave the desired para alkylation product 4.<sup>7)</sup> bp 114-115 °C (0.1 mmHg) (99%<sup>8)</sup>). Birch reduction of 4 (Li-t-BuOH-liq. NH<sub>3</sub>, ether) and subsequent hydrolysis of the resulting enol ether [(CO<sub>2</sub>H)<sub>2</sub>, H<sub>2</sub>O-DME, room temp, 25 h] gave the cyclohexenone alcohol  $5^{7)}$  (colorless oil, 68% from 4). Swern oxidation<sup>9)</sup> of 5 [DMSO-(COC1)<sub>2</sub>-Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, -60 °C to room temp, 20 min] afforded the desired aldehyde  $2^{7)}$  (colorless oil, 75%).

The spiroannelation of 2 was effected on treatment with 6 M HCl-DME (1:10) (reflux, 1 h) to produce a <u>ca</u>. 5:1 mixture of the desired spiro enone <u>3</u> and the side product <u>6</u> (97% combined yield), which could not be separated chromatographically. The mixture of <u>3</u> and <u>6</u> was oxidized directly with  $PCC^{10}$  (CH<sub>2</sub>Cl<sub>2</sub>, room temp, 2 h) to yield the spiro diketone <u>7</u><sup>7</sup> (colorless oil, 73% from <u>2</u>) and the tricyclic diketone <u>8</u><sup>7</sup> (mp 78.5-80.0 °C, 14% from <u>2</u>). The site specific reaction of 7 with dibromomethyllithium<sup>11</sup> (THF, -78 °C, 10 min) afforded a single adduct <u>9</u><sup>7</sup>, I<sub>2</sub>) (mp 153-156 °C, 98%). Reduction of <u>9</u> with Zn-AcOH<sup>13</sup> (CH<sub>2</sub>Cl<sub>2</sub>, room temp, 2 h) provided an inseparable 1:1 mixture of the bromomethylene ketones, (Z)-<u>10</u> and (E)-<u>10</u> (70%), which was reacted with methyllithium (THF, -78 °C, 1 h) to give the

Chemistry Letters, 1985



(Z)-bromomethylene alcohol (Z)- $11^{7,12,14}$  (colorless oil, 46%) and the (E)-isomer  $(E)-11^{7,12,14}$  (colorless oil, 47%). Dehydration of (Z)-11 was performed with SOCl\_-pyridine (toluene, -78 °C, 20 min) to give a 3:1 mixture of the olefins, endo-12 and exo-12 (99% combined yield).<sup>15)</sup> Finally, the mixture of endo-12 and exo-12 was oxidized with 3,5-dimethylpyrazole-CrO3 complex<sup>16)</sup> (CH<sub>2</sub>Cl<sub>2</sub>, -20 °C to  $-10 \, {}^{\circ}C$ , 1 h) to give  $(\pm) - 1^{7}$  [colorless oil, 30% from (Z)-11]. The spectral properties (IR and <sup>1</sup>H NMR) of the synthetic 1 were completely identical with those of the natural 1.

We are grateful to Professors E. Kurosawa and M. Suzuki for providing us with the spectral copies of the natural sample. Financial support from the Kurata Foundation (The Kurata Research Grant) and the Ministry of Education, Science, and Culture (Grant-in-Aid for Scientific Research No. 59470019) is acknowledged. References

- 1) Review: K. L. Erickson, "Marine Natural Products," ed by P. J. Scheuer,
- Review: K. L. Erickson, Marine Natural Products, ed by P. J. Scheder, Academic Press Inc., New York (1983), Vol. 5, Chap. 4.
   L. E. Wolinsky and D. J. Faulkner, J. Org. Chem., <u>41</u>, 597 (1976); I. Ichinose and T. Kato, Chem. Lett., <u>1978</u>, 61.
   M. Suzuki and E. Kurosawa, Tetrahedron Lett., <u>1978</u>, 4805.
   K. Yamada, M. Aratani, Y. Hayakawa, H. Nakamura, H. Nagase, and Y. Hirata, 2017 (1976) (1971)
- J. Org. Chem., <u>36</u>, 3653 (1971). 5) D. I. Schuster and W. V. Curran, J. Org. Chem., <u>35</u>, 4192 (1970).
- 6) This diol was easily prepared from δ-valerolactone by reaction with CH<sub>3</sub>MgI (ether, reflux, 4 h) in 55% yield after distillation [bp 95-97 °C (1.5 mmHg)].
  7) Satisfactory spectral (IR, <sup>1</sup>H NMR, and mass) and analytical (microanalyses or high resolution mass spectra) data were obtained for this compound.

- or high resolution mass spectra) data were obtained for this compound.
  8) All yields refer to the materials purified by silica gel column chromatography.
  9) K. Omura and D. Swern, Tetrahedron, <u>34</u>, 1651 (1978).
  10) E. J. Corey and J. W. Suggs, Tetrahedron Lett., <u>1975</u>, 2647.
  11) H. Taguchi, H. Yamamoto, and H. Nozaki, J. Am. Chem. Soc., <u>96</u>, 3010 (1974).
  12) Stereochemistry of the hydroxyl group of this compound was not determined.
  13) D. R. Williams, K. Nishitani, W. Bennett, and S. Y. Sit, Tetrahedron Lett., <u>22, 2745</u> (1981) 22, 3745 (1981).
- 14) Stereochemistry of the two isomers, (Z)-<u>ll</u> and (E)-<u>ll</u> was assigned by convert-ing the former isomer to the natural <u>l</u> in racemic form, which was previously proved to have the Z-configuration as to the bromomethylene group.<sup>3</sup>)
- 15) Isolation of endo-12 in pure form failed owing to partial isomerization of the bromomethylene group (Z+E) during separation. Thus, the final oxidation was performed without separation of the mixture of endo-12 and exo-12.
  E. J. Corey and G. W. J. Fleet, Tetrahedron Lett., 1973, 4499;
- W. G. Salmond, M. A. Barta, and J. L. Havens, J. Org. Chem., 43, 2057 (1978).

(Received August 28, 1985)

1688