

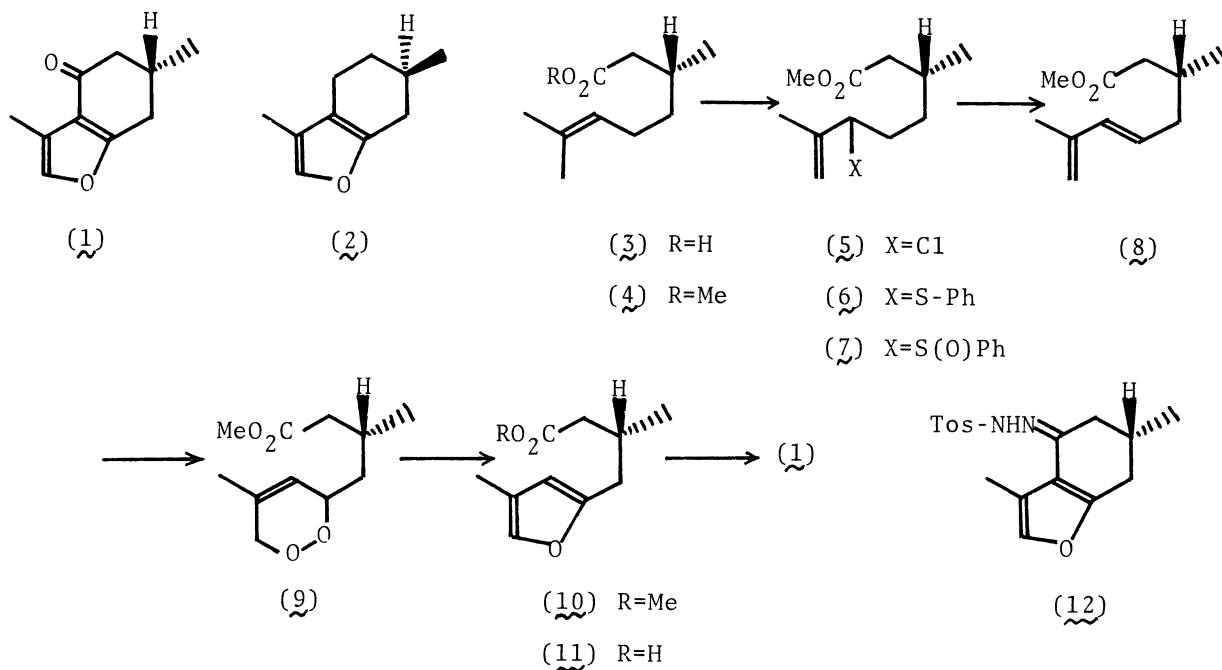
## A SYNTHESIS OF OPTICALLY ACTIVE NATURAL EVODONE

Yukio MASAKI,\* Kazuhiko SAKUMA, Kinji HASHIMOTO, and Kenji KAJI  
Gifu College of Pharmacy, 5-6-1 Mitahora Higashi, Gifu 502

(-)-Evodone, an optically active natural furano-monoterpene was synthesized from R-(+)-citronellic acid.

Evodone (1) is an optically active furano-monoterpene ketone isolated from *Evodia hortensis* FORST<sup>1</sup> and structurally closely related to menthofuran (2). Although much attention has been focused on the synthesis of evodone,<sup>2</sup> the optically active form (1) has been synthesized only by Stetter<sup>2a</sup> who resolved a racemic intermediate but has not determined the absolute configuration of the asymmetric center. Interest not only in assignment of the absolute configuration itself but also in investigation of relationship between evodone and menthofuran in biogenesis<sup>3</sup> prompted us to synthesize the optically active evodone from an optically active starting material of known absolute configuration.

Here we disclose a synthesis of natural (-)-evodone (1) from R-(+)-citronellic acid (3),<sup>4</sup> determining the absolute configuration of the former as (R), enantiomeric to natural R-(+)-menthofuran (2)<sup>5</sup> in respect to the furan-containing carbon framework.



R-(+)-Methyl citronellate (4),  $[\alpha]_D^{15} +8.0^\circ$  ( $\text{CHCl}_3$ ),<sup>6</sup> prepared by esterification of R-(+)-citronellic acid (3),  $[\alpha]_D^{15} +10.6^\circ$  ( $\text{CHCl}_3$ ),<sup>4</sup> was transformed to the terminal 1,3-diene (8) in 50% overall yield as follows; Chlorination<sup>7</sup> of (4) with 1 eq  $\text{SO}_2\text{Cl}_2$  in the presence of pyridine in  $\text{CCl}_4$  at  $0^\circ\text{C}$  for 40 min furnished the allyl chloride (5) which was converted to the allyl sulfide (6) in 80% yield on treatment with sodium thiophenoxide in DMF at  $0^\circ\text{C}$  for 1 h. Olefination was carried out by oxidation of (6) with 30%  $\text{H}_2\text{O}_2$  in AcOH followed by heating the sulfoxide (7) in toluene under reflux in the presence of  $\text{NaHCO}_3$  to give the 1,3-diene (8),  $[\alpha]_D^{15} +25.1^\circ$  ( $\text{CHCl}_3$ ), in 62% yield.

Oxidation of the diene (8) providing the furan ester (10),  $[\alpha]_D^{15} +4.2^\circ$  ( $\text{CHCl}_3$ ), was effected by photosensitized oxygenation using a high pressure mercury lamp under oxygen atmosphere in  $\text{CCl}_4$  containing a trace amount of tetraphenylporphine followed by the successive treatments of the peroxide(9) with *t*-BuOK and then with sulfuric acid in THF at  $-70^\circ\text{C}$  according to the Kondo's procedure<sup>8</sup> in 42% overall yield. After alkaline hydrolysis of the furan ester (10), cyclization<sup>9</sup> of the carboxylic acid (11) was achieved by treatment with 1 eq  $\text{PCl}_5$  and then with 1 eq  $\text{SnCl}_4$  in  $\text{CH}_2\text{Cl}_2$  at  $-5\sim 0^\circ\text{C}$  to furnish optically active evodone (1),  $[\alpha]_D^{15} -60.0^\circ$  (EtOH), mp.  $74^\circ$ , in 70% yield.

The fact that evodone thus obtained was identical in all respects involving the specific rotation with the natural one<sup>1,2</sup> and was led to enantiomeric menthofuran (enantiomer of 2),  $[\alpha]_D^{15} -91.9^\circ$  (EtOH), *via* reduction of the tosylhydrazone (12) with  $\text{NaBH}_3\text{CN}$  in THF-AcOH at  $15^\circ\text{C}$ ,<sup>10</sup> established the (R)-configuration of the asymmetric carbon in natural evodone (1).

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