

SYNTHESIS OF (-)-BIFLORA-4, 10(19), 15-TRIENE, A NOVEL
DITERPENE FROM THE DEFENSIVE SECRETION OF
CUBITERMES (TERMITE) SOLDIERS

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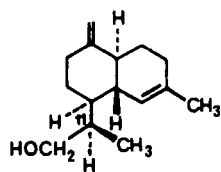
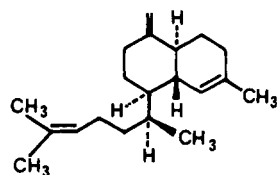
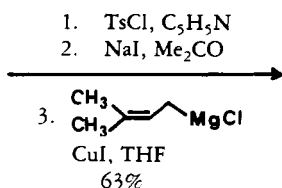
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(-)-Biflora-4, 10(19), 15-triene, a member of the rare biflorane skeletal class, was initially isolated from the frontal gland secretion of soldiers of the East African termite *Cubitermes umbratus* Williams (ca. 70 $\mu\text{g}/\text{soldier}$) (1) but has subsequently been found in the defensive secretions of several other species of *Cubitermes* soldiers (Isoptera, Termitidae, Termitinae) (2). Biflora-4, 10(19), 15-triene has also been isolated from the soft coral *Xenia obscuronata* (3). The structure and absolute stereochemistry of this novel diterpene have been shown by a combination of chemical and physical means to be as depicted in structure **1** (1,4).

In this note we report a simple preparation of (-)-biflora-4, 10(19), 15-triene from (-)-khusol [**2**], an antipodal,

**2** (-)-khusol**1** (-)-biflora-4, 10(19), 15-triene

cadinenic alcohol easily obtained from North Indian vetiver oil (5). This transformation represents, to the best of our knowledge, the first unequivocal synthesis of the natural substance.¹

¹For a possible synthesis, see Kashman and Groweiss (6). For a synthesis of the antipodal form from *R*-(+)-citronellal, see Mori and Waku (4). For total syntheses of racemic **1**, see Kodama *et al.* (7), Grieco and Nargund (8), and Parker and Farman (9). See also Vig and co-workers (10, 11).

(-)-Khusol reacted with *p*-toluenesulfonyl chloride in pyridine containing dimethylaminopyridine to yield the known tosylate (5), which, surprisingly (12, 13), returned the starting alcohol as the principal product on treatment with prenylmagnesium chloride in the presence of cuprous iodide. The corresponding iodide, however, obtained by displacement of the tosylate, reacted smoothly with the same reagents to give (-)-biflora-4, 10(19), 15-triene in 63% overall yield from khusol.^{2,3} The ¹H- and ¹³C-nmr spectra of the product were in complete agreement with those of the natural substance, which were kindly furnished by Professor D. F. Wiemer.

This synthesis, while confirming the previous assignments, makes relatively large amounts of (-)-biflora-4, 10 (19),

15-triene available for further study.

EXPERIMENTAL

(-)-BIFLORA-4, 10(19), 15-TRIENE [**1**].—The

²(-)- γ -Cadinene (5) was also formed in this reaction (25% yield). This type of reduction has previously been observed: see Marshall and Wurts (14).

³The previously undefined configuration at C-11 of (-)-khusol is, thus, *R*. [The chemical shift of the methyl at C-11 is quite different in **1** (0.74 ppm) and 11-*epi*-**1** (0.92 ppm) (4).]

rosylate (5) derived from 110 mg (0.50 mmol) of khusol [from *Vetiveria zizanioides* L. (Bharatpur origin), $[\alpha]_D^{27} -139^\circ$ ($c=3.0$, CHCl_3)] was converted conventionally to the corresponding iodide (NaI, Me_2CO , reflux). The crude product (167 mg) dissolved in 4 ml of THF was added over 1 min to a stirred mixture of 140 mg (0.74 mmol) of CuI in 8 ml (8.0 mmol) of 1 M prenylmagnesium chloride in THF at 0° under N_2 . After 1 h at 0° , the mixture was poured into saturated aqueous $\text{NH}_4\text{Cl}/\text{Et}_2\text{O}$, which was then stirred for 1 h. The crude product was isolated in the normal manner and then purified by dry silica gel chromatography with pentane to give first 26 mg (25%) of (-)- γ -cadinene (5) and then 86 mg (63%) of pure (-)-biflora-4,10(19),15-triene [**1**]: $[\alpha]_D^{20} -96^\circ$ ($c=0.16$, MeOH) [lit. (1) $[\alpha]_D -92^\circ$ ($c=0.13$, MeOH)]; ^1H nmr (CDCl_3 , 300 MHz) δ 5.53 (br s, 1H), 5.12 (br t, $J=7.1$ Hz, 1H), 4.65 (br s, 1H), 4.54 (br s, 1H), 1.69 (br s, 6H), 1.61 (br s, 3H), 0.74 (d, $J=6.9$ Hz, 3H); ^{13}C nmr (CDCl_3 , 20.1 MHz) δ 153.3, 134.7, 131.1, 125.0, 122.4, 103.2, 45.2, 44.9, 44.3, 36.4, 35.9, 31.2, 30.5, 26.9, 26.3, 25.8, 23.9, 17.7, 13.3; ir (film) 3075, 3050, 3010, 1670, 1650, 1445, 1380, 1160, 890, 835, 795 cm^{-1} ; eims m/z [$\text{M}]^+$ 272 (39%), 187 (66), 159 (39), 105 (40), 69 (53), 55 (43), 41 (100). *Anal.* calcd for $\text{C}_{20}\text{H}_{32}$: C 88.16, H 11.84, M_r 272.2504. Found: C 88.33, H 11.97, M_r (ms) 272.2504.

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