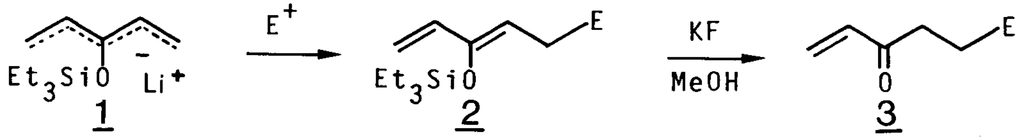
Tetrahedron Letters No. 37, pp 3505 - 3506.
©Pergamon Press Ltd. 1978. Printed in Great Britain.

0040-4039/78/0908-3505$02.00/0

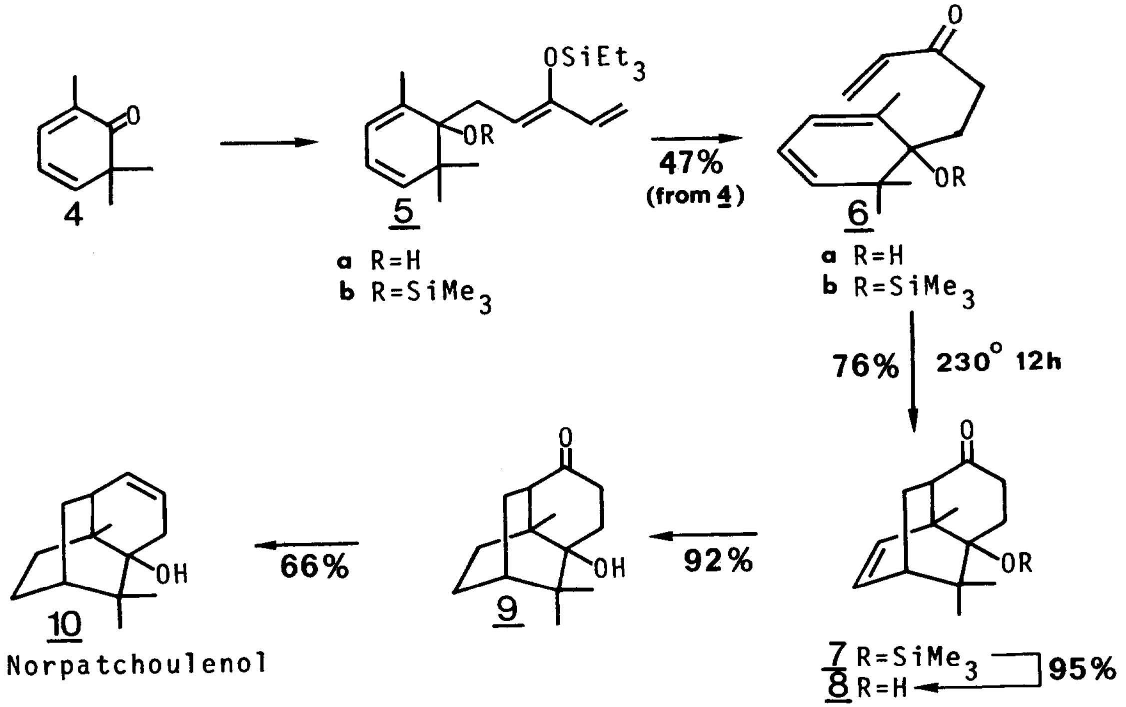
# A SHORT TOTAL SYNTHESIS OF NORPATCHOULENOL.

Wolfgang Oppolzer* and Roger L. Snowden
Département de Chimie Organique, Université de Genève, CH-1211 Genève 4.

Norpatchoulenol, a minor component of patchouli oil[1], but its main odoriferous constituent, has been shown by chemical, spectral[2] and x-ray evidence[3] to have structure 10. Its racemate was synthesized recently by a multistep approach, which included the sodium-induced cyclization of an ε-idoketone[4]. We now wish to report an alternative, more direct synthesis of (±)-10 which exploits the recently developed γ-substitution of 3-triethylsilyloxypentadienyl lithium with electrophiles, thus allowing the construction and attachment of functionalized diene and dienophile units ( 1→ 2→ 3 )[5].



Starting from the readily accessible cyclohexadienone 4[6], addition of freshly prepared 1[5] in THF at -78°/20 min. and in situ trapping of the adduct with $Me_3SiCl$ (THF/HMPT 4:1/-78°/1h) afforded the crude tetraene 5b. Selective desilylation of the enol ether was accomplished by treatment of the crude 5b with KF in methanol at 0 to 5°/1h to give, after chromatography, the vinyl ketone 6b[7] (47% overall yield from 4). On heating ( sealed tube, 0,3% in benzene/230°/12h) 6b underwent a highly regioselective intramolecular cycloaddition[8,11] to furnish the adduct 7[7] (m.p. 73-76°) in 76% yield. Desilylation[12] of 7 ($HOAc/H_2O$/THF 3:1:1/25°/10h) yielded 8[7] (m.p. 112-115°, 95%) which was hydrogenated ($PtO_2$/$H_2$(1 atm)/EtOH) to give the ketone 9[7] (m.p. 120-123°, 92%, $^1H$-NMR spectrum identical to that of naturally derived 9[2]). Successive treatment of 9 with a) 1 equiv. of $TsNHNH_2$/refluxing HOAc/10 min. and b) 3,4 equiv. of $MeLi/Et_2O$/25°/12h[13] furnished, on aqueous work-up (±)-norpatchoulenol (10)[7] (m.p. 135-141°) in 66% yield. The synthetic terpenoid (±)-10 was identified by comparison with natural (+)-norpatchoulenol using GC(coinjection), $^1H$-NMR, IR and mass spectral evidence.



Financial support of this work by Sandoz Ltd., Basel and Givaudan SA, Vernier is gratefully acknowledged. We are indebted to Dr. P. Teisseire, Roure Bertrand Dupont and to Dr. R. Kaiser, Givaudan SA for kindly providing a sample and spectra of natural (+)-norpatchoulenol and thank Mr. J.P. Saulnier and Mrs. F. Klöti for careful NMR and mass spectra measurements.

## REFERENCES

1) P. Teisseire, P. Maupetit and B. Corbier, Recherches (R.B.D.) 19, 8 (1974).
2) P. Teisseire, P. Maupetit, B. Corbier and P. Rouillier, Recherches (R.B.D.) 19, 36 (1974).
3) W.E. Oberhänsli and P. Schönholzer, Recherches (R.B.D.) 19, 62 (1974).
4) P. Teisseire, P. Pesnelle, B. Corbier, M. Plattier and P. Maupetit, Recherches (R.B.D.) 19, 69 (1974); for a partial synthesis of (+)-10 involving in vivo hydroxylation of patchoulol by rabbits see: L. Bang, G. Ourisson and P. Teisseire, Tetrahedron Lett. 1975, 2211.
5) W. Oppolzer and R.L. Snowden, Tetrahedron Lett. 1976, 4187.
6) D.Y. Curtin and A.R. Stein, Organic Synthesis 46, 115 (1966).
7) IR, $^{1}$H-NMR and mass spectra are in full agreement with the assigned structure.
8) In related Diels-Alder reactions, used as a key step in the synthesis of both (±)-patchoulenol (ref. 9) and (±)-seychellene (ref. 10), mutually reversed site selectivity was observed. For a recent review on intramolecular cycloadditions see: W. Oppolzer, Angew. 89, 10 (1977); Angew. Int. Ed. Engl. 16, 10 (1977).
9) F. Näf and G. Ohloff, Helv. 57, 1868 (1974).
10) G. Frater, Helv. 57, 172 (1974).
11) The keto alcohol 6a, obtained from 5a, did not cyclize on heating in toluene, in either absence or presence of KOtBu (ref. 9), but decomposed above 160°.
12) E.J. Corey and A. Venkateswarlu, J. Amer. Chem. Soc. 94, 6190 (1972).
13) R.H. Shapiro, Organic Reactions 23, 405 (1976).

(Received in UK 4 July 1978; accepted for publication 14 July 1978)