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A HIGHLY STEREOCONTROLLED SYNTHESIS OF (-)-KANSHONE A

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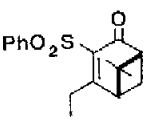
Abstract: Described herein is the first and stereoselective synthesis of (-)-kanshone A (3), a nardosinan sesquiterpere, starting with enone 2.

In the preceding paper,[1] we reported that allylation of enone 1, derived from (+)-nopinone, with allyl bromide proceeded in an extracyclic stereocontrolled fashion to give enone 2 in synthetically satisfied yield. In order to study use of 2 in natural product synthesis, (-)-kanshone A (3), a nardosinan sesquiterpene isolated from Nardostachys chinensis,[2] was chosen as the first target molecule. We wish to describe here the highly stereocontrolled and first total synthesis of 3.



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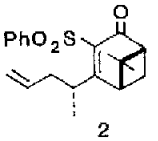

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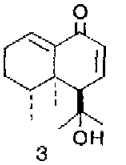


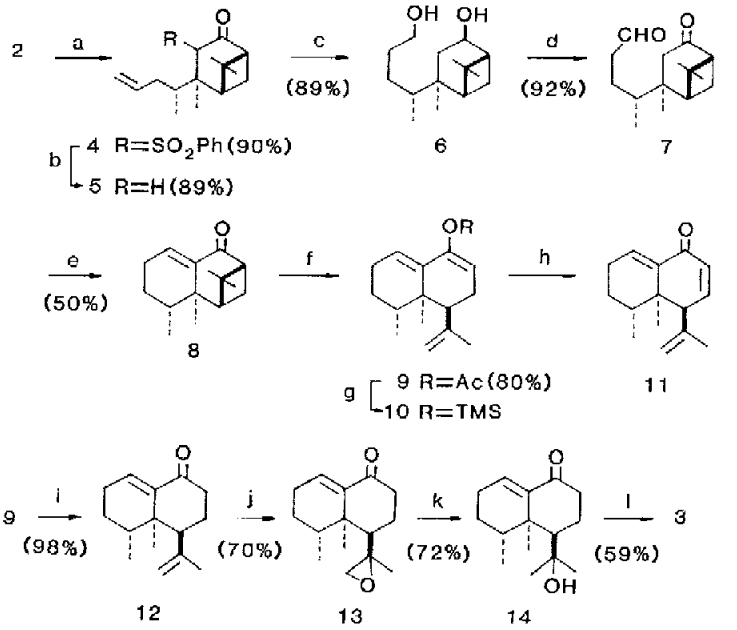
3

Treatment of 2 with Me_2CuLi led to stereoselective Michael addition to give the adduct 4, which on desulfurization provided 4,4-disubstituted nopinone 5 (Scheme 1). Hydroboration-oxidation of 5 followed by Swern oxidation of the resulting diol 6 afforded keto-aldehyde 7, and cyclization of the latter with $KOBu^t$ gave the tricyclic enone 8 in fair yield.

$BF_3 \cdot OEt_2$-promoted cyclobutane cleavage[3] in 8 gave high yield of enol acetate 9 which possesses the nardosinan carbon skeleton with correct stereochemistry. Conversion of 9 to enol silyl ether 10 followed by palladium catalyzed dehydrosilylation[4] provided cross-conjugated dienone 11 whose physical data including the sign of the specific rotation were identical with those of authentic 11 derived from natural 3.[2]

Regioselective epoxidation of dienone 12 prepared from hydrolysis of 9 was performed by treatment with mCPBA (1 equiv) to give epoxide 13, whose lithium aluminum hydride reduction in refluxing THF followed by PDC oxidation gave dihydrokanshone A (14). Finally, transformation of 14

to 3 was accomplished by phenylselenenylation and subsequent selenoxide elimination. IR and ^{1}H NMR data of the synthetic 3 (crystals, mp 96-98 °C), $[\alpha]^{20}_D$ -245.1° (c 0.39, $CHCl_3$)[5] were in good accordance with those of natural 3 (oil), $[\alpha]_D$ -147.8° (c 0.35, $CHCl_3$)[5], in all respects.[2,6]



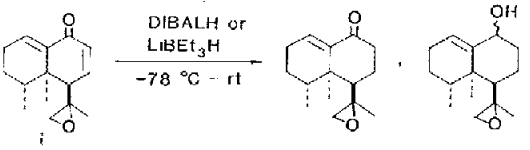
a) Me_2CuLi, THF; b) Na(Hg), MeOH; c) B_2H_6, THF, then 30% H_2O_2, aq NaOH; d) DMSO, $(COCl)_2$, CH_2Cl_2, then Et_3N; e) t-BuOK, CH_2Cl_2, rt, 20 min; f) BF_3·OEt_2, $Zn(OAc)_2$, Ac_2O; g) MeLi, TMSCl, HMPA, Et_2O; h) $Pd(OAc)_2$, MeCN; i) K_2CO_3, MeOH; j) mCPBA, CH_2Cl_2; k) (i) $LiAlH_4$, THF, reflux, (ii) PDC, CH_2Cl_2; l) (i) $(TMS)_2NLi$, PhSeCl, HMPA, THF, (ii) 30% H_2O_2, Py, THF.

Scheme 1

Acknowledgment: We are grateful to Dr. Y. Oshima for providing us ^{1}H NMR and IR spectra of (-)-kanshone A.

References and Notes

1 Kato, M.; Watanabe, M.; Awen, B. Z.; Vogler, B.; Yoshikoshi, A. Tetrahedron Lett. **1991**,
2 Bagchi, A.; Oshima, Y.; Hikino, H. Phytochemistry, **1988**, 27, 1199.
3 Kato, M.; Kamat, V. P.; Tooyama, Y.; Yoshikoshi, A. J. Org. Chem. **1989**, 54, 1536.
4 Tto, Y.; Hirano, T.; Saegusa, T. J. Org. Chem. **1978**, 43, 1011.
5 The difference of specific rotation between natural and synthetic 3 arises from impurities contaminated in natural 3 as a result of difficulty of purification (private communication).
6 Attempts to synthesize 3 by reductive cleavage of the oxirane in epoxy dienone i derived from regioselective epoxidation of 11 failed because the oxirane was unreactive under the conditions shown below.



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