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Radical Cyclization of β-Alkoxyacrylates: Stereoselective Synthesis of (-)-*trans*-Kumausyne†

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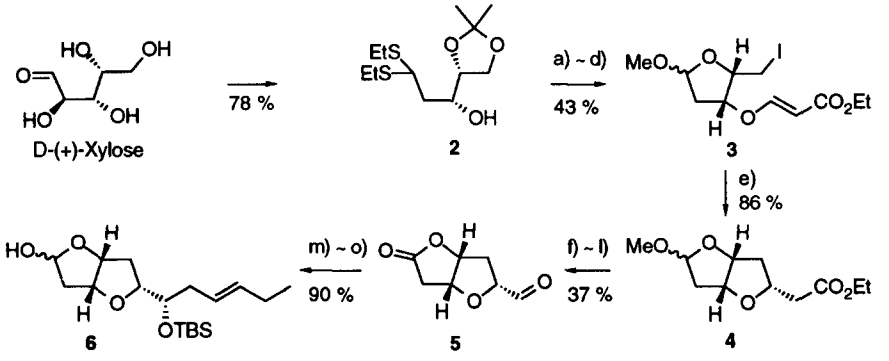
Abstract : (-)-*trans*-Kumausyne was synthesized from D-(+)-xylose. Radical cyclization reaction of a β-alkoxyacrylate intermediate proceeded stereoselectively to give a tetrahydrofuranyl product with correct stereochemistry. © 1997 Elsevier Science Ltd.

(-)-*trans*-Kumausyne (**1**) was isolated from the red alga *Laurencia nipponica* Yamada by Kurosawa and coworkers.[1] The first total synthesis of (±)-*trans*-kumausyne was achieved by Overman, in which the pivotal *cis*-hydrobenzofuranone intermediate was obtained from 1-vinylcyclopentane-1,2-diol and α-(benzyloxy)-acetaldehyde via Prins-pinacol rearrangement strategy.[2] More recently, Sugimura reported a total synthesis of (-)-*trans*-kumausyne utilizing the stereoselective formation of substituted tetrahydrofurans in the BF_3-promoted reaction of 2,3-*O*-isopropylidene derivatives of *aldehydo*-aldose with allylsilanes.[3]

We reported some time ago that *cis*-2,5-disubstituted tetrahydrofurans and *cis*-2,6-disubstituted tetrahydropyrans are stereoselectively obtained via radical cyclization of β-alkoxyacrylates.[4] Our interest in **1** originated from the *cis*-2,5-disubstituted tetrahydrofuran motif present, and we now wish to report a total synthesis of **1** based on radical cyclization.

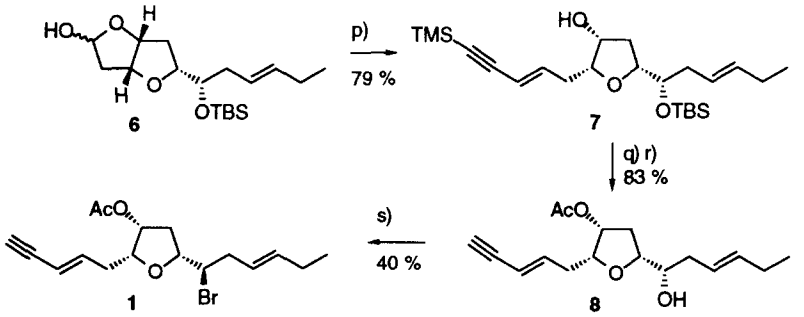


a) $HCCCO_2Et$, NMM, DCM, r.t.; b) p-TsOH, MeOH, r.t. 30 min/1.3 eq. $PhI(TFA)_2$, r.t. 2 h
c) p-TsCl, Pyridine, 0 °C; d) 1.5 eq. TBAI, Toluene, Reflux
e) 1.4 eq. Bu_3SnH, 0.1 eq. AIBN, Benzene (0.02 M), Reflux, 4 h , (Syringe Pump, 3 h)
f) LAH, THF, 0 °C; g) p-TsCl, Pyridine, 0 °C; h) PhSeNa, EtOH, Reflux; i) H_2O_2, EtOH, Reflux
j) Jones Reagent, Acetone; k) OsO_4, NMO, aq. Acetone; l) $Pb(OAc)_4$, Na_2CO_3, DCM, 0 °C
m) 2.0 eq. $CH_2CHCH(TMS)CH_2CH_3$, $BF_3{\cdot}OEt_2$, DCM, -78 °C ~ r.t.
n) TBDMSCl, cat. DMAP, Imidazole, DCM, Reflux; o) DIBAL, Toluene, -78 °C

Scheme 1

† **Dedicated to Professor Dieter Seebach on the occasion of his 60th birthday.**

The dithioacetal **2**, prepared from D-(+)-xylose in four steps,[5] was converted into the β-alkoxyacrylate **3** via reaction with ethyl propiolate, deprotection with concomitant cyclic acetal formation, tosylation, and iodide substitution. The β-alkoxyacrylate **3** was reacted with tributylstannane under the standard high dilution conditions to yield the bicyclic tetrahydrofuran **4** as the only cyclization product (Scheme 1). The conversion to the corresponding vinyl derivative involved reduction, tosylation, phenyl selenide substitution, and selenoxide elimination, and it was oxidized to the lactone[6] before oxidative removal of one carbon to yield the aldehyde lactone **5**. Sakurai reaction of **5** with 3-(trimethylsilyl)-1-pentene,[2] TBS protection, and DIBAL reduction led to the isolation of the bicyclic hemiacetal **6** in good yield.



(-)-*trans*-Kumausyne

p) 8.0 eq. TMSCCCH=PPh_3, THF, -78 °C ~ r.t. 6 h
q) Ac_2O, Pyridine, r.t.; r) TBAF, THF, r.t. 24 h
s) 4.8 eq. CBr_4, 4.8 eq. Ph_3P, 2.4 eq. Pyr-2,6-t-Bu_2, Benzene, 40 °C, 20 min

Scheme 2

Addition of a three carbon segment to **6** to form the enyne moiety was achieved via reaction with (3-trimethylsilyl-2-propynyl)-triphenylphosphorane[7] to yield **7**. Acetylation and removal of silyl protecting groups afforded the secondary alcohol **8** in good yield. Finally, (-)-*trans*-kumausyne (**1**)[8] was obtained via bromide substitution on **8** under the reaction conditions reported by Overman[2] (Scheme 2).

The present synthesis is conceptually straightforward and it provides another example in the stereoselective preparation of oxacycles via radical cyclization of β-alkoxyacrylates. Further developments in these directions will be reported in due course.

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REFERENCES

1. Suzuki, T.; Koizumi, K.; Suzuki, M.; Kurosawa, E. *Chem. Lett.* **1983**, 1643-1644.
2. Brown, M. J.; Harrison, T.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5378-5384.
3. Osumi, K.; Sugimura, H. *Tetrahedron Lett.* **1995**, *36*, 5789-5792.
4. a) Lee, E.; Tae, J. S.; Lee, C.; Park, C. M. *Tetrahedron Lett.* **1993**, *34*, 4831-4834. b) Lee, E.; Tae, J. S.; Chong, Y. H.; Park, Y. C.; Yun, M.; Kim, S. *Tetrahedron Lett.* **1994**, *35*, 129-132. c) Lee, E.; Park, C. M. *J. Chem. Soc. Chem. Comm.* **1994**, 293-294. d) Lee, E.; Park, C. M.; Yun, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 8017-8018.
5. Rollin, P.; Pougny, J. R. *Tetrahedron*, **1986**, *42*, 3479-3490.
6. The cyclic acetal function did not survive the subsequent Sakurai reaction.
7. Corey, E. J.; Ruden, R. A. *Tetrahedron Lett.* **1973**, *14*, 1495-1499.
8. $[\alpha]_D^{28}$=-2.2 °(*c* 0.28, $CHCl_3$); lit.[1] $[\alpha]_D^{26}$=-2.3 °(*c* 0.62, $CHCl_3$)

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