Pergamon

Tetrahedron Letters 41 (2000) 4401–4402

TETRAHEDRON
LETTERS

Concise synthesis of anolignan A

Meiming Luo, Akiko Matsui, Tomoyuki Esumi, Yoshiharu Iwabuchi and
Susumi Hatakeyama*

Faculty of Pharmaceutical Sciences, Nagasaki University, Nagasaki 852-8521, Japan

Received 21 March 2000; revised 6 April 2000; accepted 7 April 2000

Abstract

An efficient synthesis of anolignan A has been achieved in eight steps in 30% overall yield from piperonal employing $TiCl_4$-mediated addition of a 1-trimethylsilyl-2,3-butadiene to an aldehyde as the key step.

Keywords: lignans; silicon compounds; 1-trimethylsilyl-2,3-butadienes; addition reactions.

Anolignan A was isolated from *Anogeissus acuminata* as an active HIV-1 reverse transcriptase inhibitory constituent by bioassay-guided fractionation.[1] Recently, we have developed an efficient method for the preparation of substituted 1,3-butadienes employing 1-trimethylsilyl-2,3-butadienes.[2,3] The characteristic unsymmetrical 2,3-disubstituted 1,3-butadiene structure as well as its interesting biological activity prompted us to investigate a total synthesis of anolignan A based on this methodology. We report herein the first synthesis of anolignan A.

Piperonal **1** was first converted into propargyl alcohol **3** via acetate **2** by a three-step sequence involving propargylation using tetrahydro-2-(2-propynyloxy)-2*H*-pyran, acetylation, and removal of the benzylic acetoxy group with TFA–Et_3SiH in 65% overall yield. Several attempts to obtain **3** by direct alkylation of tetrahydro-2-(2-propynyloxy)-2*H*-pyran with piperonyl chloride failed. After tosylation of **3**, reaction[3] of tosylate **4** with trimethylsilylmethylmagnesium chloride in the presence of CuCN and LiCl produced 1-trimethylsilyl-2,3-butadiene **5** selectively in good yield. $TiCl_4$-mediated addition of **5** to 2,4-diacetoxybenzaldehyde in the presence of acetonitrile (1 equiv.) proceeded smoothly with concomitant acyl migration to give 1,3-butadiene **6**. In this particular case, addition of acetonitrile was found to be of critical importance for this successful transformation, because compound **6** was not obtained in the absence of acetonitrile.[†] Possibly the Lewis acidity of $TiCl_4$ was appropriately attenuated by complexation with acetonitrile so that

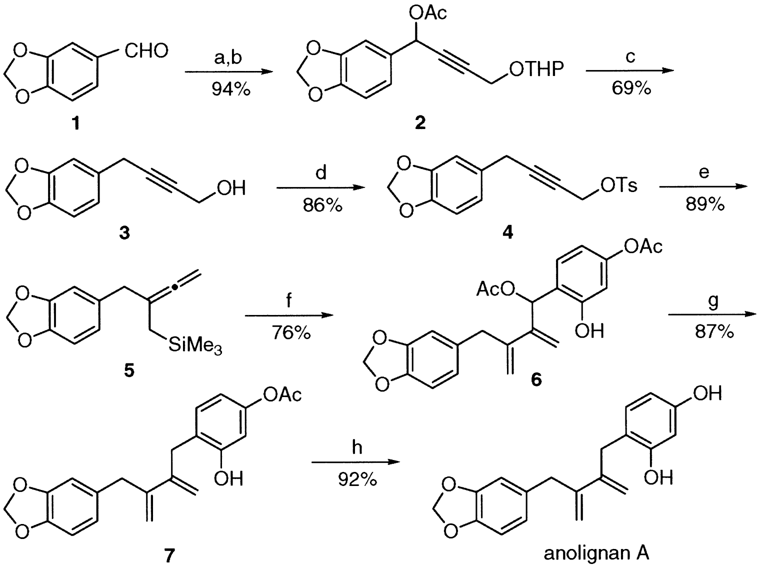
---

* Corresponding author. Tel: +81 95 847 1111; fax: +81 95 848 4286; e-mail: susumi@net.nagasaki-u.ac.jp

[†] Reaction of benzaldehyde with 1-trimethylsilyl-2,3-butadiene was found to be unsuccessful when $TiCl_4$ was used as the catalyst alone, see: Hatakeyama, S.; Sugawara, K.; Kawamura, M.; Takano, S. *Tetrahedron Lett.* **1991**, *32*, 4509–4512.

PII: S0040-4039(00)00604-3

the resulting acid-labile **6** was obtained without decomposition. Upon treatment of **6** with HCO_2H–Et_3N in the presence of $PdCl_2(PPh_3)_2$ (3 mol%) in boiling dioxane,[4] the reductive removal of the benzylic acetoxy group took place with complete regioselectivity to give **7** exclusively. Finally, saponification of **7** furnished anolignan A as colorless needles, mp 97–98°C (CH_2Cl_2),[‡] which exhibited spectral properties (^1H and ^{13}C NMR, IR, MS) in accord with those[1] reported (Scheme 1).



Scheme 1. *Reactions and conditions*: (a) tetrahydro-2-(2-propynyloxy)-2*H*-pyran, *n*-BuLi, THF, –78°C; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (c) Et_3SiH, TFA, CH_2Cl_2, –20°C; (d) *n*-BuLi, TsCl, THF, –40°C; (e) Me_3SiCH_2MgCl (3 equiv.), CuCN (3 equiv.), LiCl (6 equiv.), THF, –40°C; (f) 2,4-diacetoxybenzaldehyde, $TiCl_4$ (1 equiv.), CH_3CN (1 equiv.), CH_2Cl_2, –78°C; (g) HCOOH (10 equiv.), Et_3N (10 equiv.), $PdCl_2(PPh_3)_2$ (3 mol%), dioxane, reflux; (h) 5% NaOH, MeOH

In conclusion, the present work illustrates a new methodology for the synthesis of dibenzylbutadiene lignans as well as the synthetic utility of 1-trimethylsilyl-2,3-butadienes.

Acknowledgements

This work was supported by a JSPS postdoctoral fellowship for M.L.

References

1. Rimando, A. M.; Pezzuto, J. M.; Fransworth, N. R. *J. Nat. Prod.* **1994**, *57*, 896–904.
2. Hatakeyama, S. *J. Synth. Org. Chem. Jpn.* **1997**, *55*, 793–802.
3. Nishiyama, T.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Tetrahedron Lett.* **1998**, *39*, 43–46.
4. Tsuji, J.; Minami, I.; Shimizu, I. *Synthesis* **1986**, 623–627.

[‡] The melting point was not reported in the literature.