Tetrahedron Letters, Vol.32, No.10, pp 1325-1326, 1991 Printed in Great Britain

## AN EXTREMELY SHORT SYNTHESIS OF THE PROSTAGLANDIN KEY INTERMEDIATE THROUGH A NOVEL VINYL ANION EQUIVALENT

Shinya Kusuda, Yoshihiko Watanabe, Yoshio Ueno, and Takeshi Toru<sup>\*</sup> Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466, Japan

Summary: A one-pot synthesis of the  $\text{PGE}_2$  key intermediate from 2-(phenyl-seleno)-2-cyclopentenone is described.

Sih and his collaborators have developed an excellent 2-component coupling process for the construction of the prostaglandin (PG) skeleton<sup>1</sup>. However, only a few syntheses of the chiral cyclopentenone intermediate have been reported.<sup>2</sup> We now report an extremely short, convenient, and efficient synthesis of the optically active prostaglandin intermediate through a novel vinyl anion equivalent carrying adjacent seleno and stannyl groups.



The reaction consists of three consecutive procedures;  $\beta$ -addition of 2-(phenylseleno)-cyclopentenone, tributylstannyllithium to the regiospecific alkylation of the resulting enolate, and subsequent novel regiospecific  $\beta$ -elimination of adjacent tin and seleno groups. The starting hydroxyselenocyclopentenone $^3$  2 is silyl-protecting optically active from chiral silyloxycyclopentenone<sup>4</sup> 1 in 95% yield. obtainable A tetrahydrofuran (THF) solution of the selenocyclopentenone 2 was treated at -78 °c with tributylstannyllithium (2.0 equiv) prepared in situ from hexabutyldistannane and n-butyllithium.<sup>5</sup> After stirring for 5 min, methyl 7-iodo-5-heptenoate (2.0 equiv) and hexamethylphosphoramide (4.0 equiv) The mixture was stirred for 15 min. were added successively. The chemoselective  $\beta$ -elimination of stannyl and phenylseleno groups was achieved by the action of tetrabutylammonium fluoride (TBAF). This stage, however, is crucial, because the silyl protecting group sensitive to a fluoride ion is present in the molecule. In fact, treatment of the reaction mixture with excess TBAF (3 equiv) gave 4-hydroxycyclopentenone 5a in 79% yield. The tributylstannyl group was observed to be more sensitive



5b R = Si  $\leq$  : 86% based on 1

to the fluoride ion than the (tert-butyldimethylsilyi)oxy group as follows. Careful addition of a TBAF THF solution by 4 portions (totally 2 equiv) afforded the desired sily1-protected intermediate 5b in 67% yield. More effective destannylselenenylation was achieved by the action of silica gel. Thus, the silica gel, absorbing the reaction mixture, was heated at 45  $^{
m O}{
m C}$ for 2 h to give  $5b^6$  in 86% yield, i.e. in 80% overall yield from 1.

One of the advantageous features of this method is that regiospecific alkylation of the enolate (without enolate equilibration and elimination of protected 4-hydroxy group) and regiospecific formation' of the the endocyclic enone can be achieved. Furthermore, the three-step procedure can be performed in one pot. Thus, the present reaction serves an exceptionally rapid, convenient, and efficient method for the synthesis of the chiral PGE, key intermediate, starting with chiral protected 4hydroxycyclopentenone through a novel vinyl anion equivalent.

## References and notes

- (1) J. B. Heather, R. Sood, P. Price, G. P. Peruzzotti, S. S. Lee, and C. J. Sih, Tetrahedron Lett., 1973, 2313; C. J. Sih, J. B. Heather, G. P. Peruzotti, P. Price, R. Sood, and L. F. Hsu Lee, J. Am. Chem. Soc., 95, 1676 (1973).
- (2) (a) S. Okamoto, Y. Kobayashi, H. Kato, K. Hori, T. Takahashi, J. Tsuji, and F. Sato, J. Org. Chem., 53, 5590 (1988); (b) C. J. Sih, J. B. Heather, R. Sood, P. Price, G. Peruzzotti, L. F. Hsu Lee, and S. S. Lee, J. Am. Chem. Soc., 97, 865 (1975); (c) G. Stork, C. Kowalski, and G. Garcia, J. Am. Chem. Soc., 97, 3258 (1975).
  (3) T. Toru, Y. Yamada, T. Ueno, E. Maekawa, and Y. Ueno, J. Am. Chem. Soc., 110, 4815 (1988).
- (4) M. Kitamura, K. Manabe, R. Noyori, and H. Takaya, Tetrahedron Lett., 28, 4719 (1987) and ref cited therein.
- (5) W. C. Still, J. Am. Chem. Soc., 99, 4836 (1977).
  (6) [α]<sup>25</sup> +15.5° (c 1.32, MeOH). 5a obtained by desilylation of 5b: [α]<sup>29</sup> +12.6° (c 0.94, MeOH) [lit.2b [α]<sup>23</sup> +12.4° (c 0.91, MeOH)].
  (7) We have observed that the deselenenylation of 2-allyl-2-(phenyl-color) and the deselenenylation of 2-allyl-2-(phenyl-color).
- seleno)cyclopentan-1-one through oxidation with hydrogen peroxide at 0 °C gives a 81:19 mixture of exocyclic and endocyclic enones, see also: D. Liotta, C. S. Barnum, and M. Saindane, J. Org. Chem., 46, 4301 (1981); G. Zimma, C. S. Barnum, and D. Liotta, J. Org. Chem., 45, 2737 (1980).

(Received in Japan 29 November 1990)