12.5 Hz, C(11) H), 4.77 (d, 1 H, J = 5 Hz, C(16) H), 3.80 (br s, 1 H, C(7) H), 3.73 (dd, 1 H, J = 12.5, 6.0 Hz, C(2) H)]. Compound **10** was smoothly transformed (50% yield) upon treatment with sodium methoxide in dimethyl sulfoxide [55 °C (30 min), 95 °C (1 h)] under argon[12] into bis(diosphenol) **11** (R = H),[8] mp 207–209 °C [IR ($CHCl_3$) 3450, 1680, 1650 cm^{-1}; ^1H NMR (220 MHz) ($CDCl_3$) δ 5.68 (d, 1 H, J = 3 Hz, C(3) olefinic proton), 3.25 (s, 1 H, C(9) α-H), 1.84 (s, 3 H, C(13) methyl group)], possessing the desired configuration at C(9). In a subsequent step methylation (NaOMe, Me_2SO, MeI) of **11** (R = H) gave rise to **11** (R = Me),[8] mp 214–216 °C [^1H NMR (220 MHz) ($CDCl_3$) δ 3.59 (s, 3 H), 3.54 (s, 3 H), 3.34 (s, 3 H)], in 65% yield. The two-step conversion of **10** into **11** (R = Me) could be achieved in a single operation [NaOMe (40 equiv), Me_2SO–MeOH (10:1), 55 °C (30 min), 95 °C (1 h), 10 °C, MeI (15 min)] providing neoquassin β-*O*-methyl ether (**11**) (R = Me)[8] in 57% overall yield.

Selective hydrolysis [HOAc–HOH (3:2), reflux, 25 min] of the protected lactol in **11** (R = Me) afforded crystalline racemic neoquassin (**2**) identical with a sample of natural neoquassin by comparison of spectral properties [^1H NMR (220 MHz), IR] and thin-layer mobility in several solvent systems. Oxidation (Fetizon's reagent,[13] benzene, 2 h, reflux) of synthetic neoquassin provided in 77% yield from **11** (R = Me) racemic quassin, mp 189–190 °C. The overall yield of **1** from enone **3** was 2.9%. Synthetic quassin (**1**) was identical with an authentic sample by TLC, IR, and ^1H NMR (220 MHz).

Acknowledgment. This investigation was supported by a Public Health Service Research Grant (CA 28865) from the National Cancer Institute and, in part, by G. D. Searle and Co. We are grateful to Dr. K. Kanai for experimental contributions during the very early stages of the synthesis.

(12) Attempts to carry out the transformation of **10** into **11** in an atmosphere of oxygen lead to decomposition of the intermediate diosphenols.
(13) Fetizon, M.; Golfier, M. *C. R. Acad. Sci., Ser. C* **1968**, *267*, 900.
(14) On leave from the University of Pavia, 1979–1980.

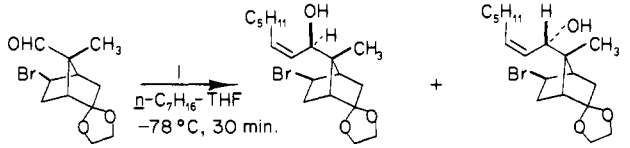
Paul A. Grieco,* Sergio Ferriño, Giovanni Vidari[14]
Department of Chemistry, Indiana University
Bloomington, Indiana 47405
Received July 17, 1980

Complete Transfer of Chirality in the [3,3]-Sigmatropic Rearrangement of Allylic Acetates Catalyzed by Palladium(II). Application to Stereocontrolled Syntheses of Prostaglandins Possessing either the C-15(*S*) or C-15(*R*) Configuration

Sir:

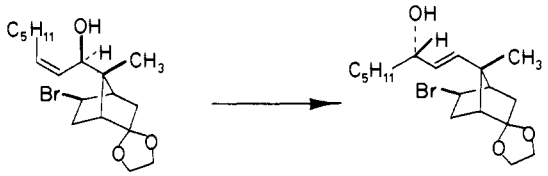
Considerable effort has been expended during the past 10 years on the development of synthetic approaches to prostaglandins which control stereochemistry at C-15.[1] Interest in both natural and C-15 epi prostaglandins[2] has led us to devise a practical, stereocontrolled approach to prostaglandins possessing either the C-15(*S*) or C-15(*R*) configuration. We detail below the results of our investigation which addressed the question of chirality transfer in the palladium(II)-catalyzed sigmatropic rearrangement of allylic acetates.[3]

Our observation that 1-lithio-1-*cis*-heptene (**1**)[4a] adds in a highly stereoselective fashion to aldehyde **2**,[4b,6] giving rise to an 81% yield



2 3 4

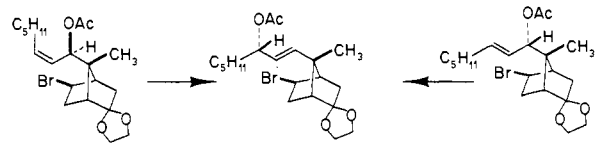
of allylic alcohol **3** [R_f 0.48 (1:1 ether–hexane)] and an 8% yield of the isomeric alcohol **4** (R_f 0.35), suggested the possibility of a stereocontrolled approach to elaboration of the ω side chain of prostanoids. Of critical importance to such a plan would be the ability to effect a complete, concerted allylic oxygen interconversion (C–O → C–O chirality transfer; cf. **3** → **5**). Although it has



3 5

been established that catalytic amounts of palladium(II) salts will equilibrate allylic acetates,[3b] no reports dealing with transfer of chirality have appeared in the literature.[7]

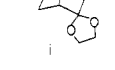
Allylic alcohol **3** was converted [Ac_2O, Py, DMAP,[8] CH_2Cl_2 (96% yield)] into allylic acetate **6** and treated (25 °C) with a catalytic amount of bis(acetonitrile)palladium(II) chloride (0.04 equiv) in tetrahydrofuran for 3.5 h. *Workup provided a 91% yield of a single rearranged allylic acetate*, **7**. That **7** possessed the



6 7 8

structure shown was unambiguously established by conversion[9]

(1) Corey, E. J.; Albonico, S. M.; Koelliker, U.; Schaaf, T. K.; Varma R. K. *J. Am. Chem. Soc.* **1971**, *93*, 1491. Corey, E. J.; Becker, K. B.; Varma, R. K. *Ibid.* **1972**, *94*, 8616. Iguchi, S.; Nakai, H.; Hayashi, M.; Yamamoto, H. *J. Org. Chem.* **1979**, *44*, 1363. Noyori, R.; Tomino, I.; Nishizawa, M. *J. Am. Chem. Soc.* **1979**, *101*, 5843. Also see: Sih, J. C.; Price, P.; Sood, R.; Salomon, R. G.; Peruzzotti, G.; Casey, M. *Ibid.* **1972**, *94*, 3643. Kluge, A. F.; Untch, K. G.; Fried, J. H. *Ibid.* **1972**, *94*, 7827. Pappo, R.; Collins, P. W. *Tetrahedron Lett.* **1972**, 2627. Bernady, K. F.; Poletto, J. F.; Weiss, M. J. *Ibid.* **1975**, 765. Stork, G.; Takahashi, T.; Kawamoto, I.; Suzuki, T. *J. Am. Chem. Soc.* **1978**, *100*, 8271.
(2) Fried, J.; Lin, C. H. *J. Med. Chem.* **1973**, *16*, 429. Grieco, P. A.; Owens, W.; Wang, C.-L. J.; Williams, E.; Schillinger, W. J. *J. Med. Chem.* **1980**, *23*, 1072. Grieco, P. A.; Schillinger, W. J.; Yokoyama, Y. *Ibid.* **1980** *23*, 1077.
(3) (a) Henry, P. M. *J. Am. Chem. Soc.* **1972**, *94*, 5200. (b) Overman, L. E.; Knoll, F. M. *Tetrahedron Lett.* **1979**, 321.
(4) (a) The vinyllithium derivatives **1** and **9** were prepared by treatment of 1-iodo-1-*cis*-heptene [Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086] and 1-iodo-1-*trans*-heptene [Zweifel, G.; Whitney, C. C. *Ibid.* **1967**, *89*, 2753], respectively, with *n*-butyllithium in heptane at ~−78 °C. (b) Aldehyde **2** was prepared by Collins oxidation of the corresponding alcohol whose synthesis has been detailed on a previous occassion.[5]
(5) Grieco, P. A.; Pogonowski, C. S.; Burke, S. D.; Nishizawa, M; Miyashita, M.; Masaki, Y.; Wang, C.-L. J.; Majetich, G. *J. Am. Chem. Soc.* **1977**, *99*, 4111.
(6) We have also observed that addition of an ethereal solution of methyl lithium to aldehyde **2** at −78 °C gave rise to an 83% isolated yield of alcohol



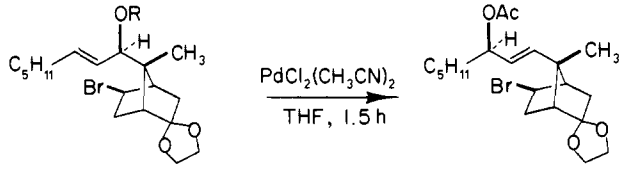
i

i, mp 127.0–127.5 °C, whose structure was established by single-crystal X-ray analysis (unpublished results, George Majetich).
(7) Professors Eschenmoser and Overman (private communication) have independently examined the question of chirality transfer during the palladium(II)-catalyzed rearrangement of allylic acetates and have arrived at very similar conclusions.
(8) Hofle, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.

0002-7863/80/1502-7587$01.00/0

into 12-methyl-$PGF_{2\alpha}$, identical with a sample prepared on a previous occassion[5] by comparison of spectral properties (^1H NMR, IR) and TLC mobility in several solvent systems. It is important to note that the success of the transformation of **6** into **7** was dependent not only on the suprafacial nature of the palladium(II) catalyzed rearrangement but also upon the exclusive preference for *trans*-allylic acetate **7** over *trans*-allylic acetate **8**, since under the reaction conditions the catalyst would be expected to set up an equilibrium between **7** and **8** as well. The exclusive formation of **7** during the conversion of **6** → **7** is undoubtedly due to the conformational rigidity of the bicyclo[2.2.1]heptane ring system coupled with the presence of the bulky C(5) exo-oriented bromine atom and the C(7) methyl group. The highly encumbered C(13) carbon atom (prostaglandin numbering) minimizes steric congestion by preferring sp^2 over sp^3 hybridization, thus driving the equilibrium in favor of **7**.

In a second series of experiments, 1-lithio-1-*trans*-heptene (**9**)[4a] was added to aldehyde **2** affording an 87% isolated yield of allylic alcohol **10**, R_f 0.58 (1:1 hexane–ether).[11] Acetylation of **10**



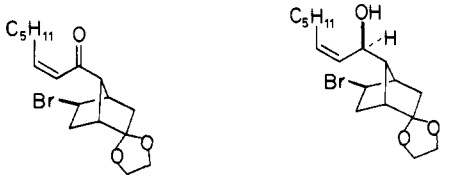
10, R = H

11, R = Ac

12

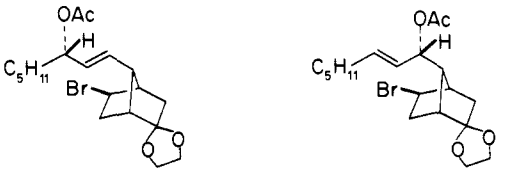
followed by rearrangement provided (93%) as the sole product allylic acetate **12**. The identity of **12** was unambiguously established by transformation into 15-epi-12-methyl-$PGF_{2\alpha}$.[5]

Additional experimentation substantiated the results described above concerning chirality transfer. Allylic alcohol **14**, *prepared*



13 14

in 84% isolated yield by reduction [$LiAlH(OCH_3)_3$,[12] *THF, −100 °C*] *of cis-enone* **13**,[13] was converted into the corresponding acetate and subjected to the rearrangement conditions [$PdCl_2(CN_3CN)_2$, THF, 2 h]. There was obtained in 90% yield an 85:15 mixture, respectively, of the desired *trans*-allylic acetate **15**[14] and the C(13) *trans*-allylic acetate **16**. The observed ratio of **15**:**16** is not totally unexpected in view of the decreased steric congestion about C(13)

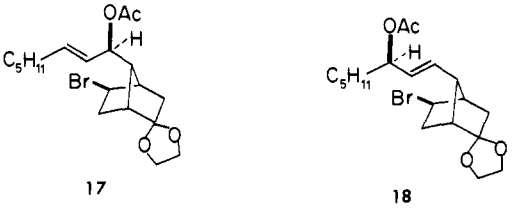


15 16

relative to the example described above (cf. **7** and **8**), where C(13) is pseudoneopentyl in nature.

It was indeed reassuring to find that the same 85:15 ratio of **15**:**16** which was achieved above under equilibrating conditions employing the *cis*-allylic acetate corresponding to **14** could also be realized by using an authentic sample of pure *trans*-allylic acetate **16**.[13]

Similarly the acetate **17**[13] gave way under equilibrating con-



17 18

ditions to a 86:14 mixture, respectively, of the rearranged allylic acetate **18** and starting acetate **17**.

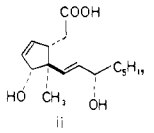
It is clear from the studies above that one can rely upon the palladium(II)-catalyzed [3,3]-sigmatropic rearrangement of allylic acetates for the facile transfer of chirality. In particular, the methodology offers a mild, general solution to the problem of controlling stereochemistry at "C(15)" in rigid bicyclo[2.2.1]-heptane intermediates along the pathway to prostaglandins.

Acknowledgment. Generous support of this work by the National Institute of Child Health and Human Development, National Institutes of Health (Grant HD 14646), and G. D. Searle and Co. is gratefully acknowledged.

Paul A. Grieco,* Tetsuo Takigawa
Shannon L. Bongers, Hideo Tanaka
Department of Chemistry, Indiana University
Bloomington, Indiana 47405

Received August 4, 1980

(9) Compound **7** was smoothly transformed [(a) K_2CO_3, MeOH; (b) DBU, DMF, 160 °C, 16 h; (c) 10% HCl–THF (1:3); (d) H_2O_2, NaOH, MeOH, 0–5 °C, 24 h] into hydroxy carboxylic acid ii which was taken to



ii

12-methyl-$PGF_{2\alpha}$ by conventional means.[10]

(10) Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5676. Grieco, P. A.; Yokoyama, Y.; Withers, G. P.; Okuniewicz, F. J.; Wang, C.-L. J. *J. Org. Chem.* **1978**, *43*, 4178.

(11) In addition, approximately 10% of the corresponding isomeric allylic alcohol (R_f 0.39) was isolated.

(12) Brown, H. C.; Hess, H. M. *J. Org. Chem.* **1969**, *34*, 2206.

(13) The straightforward preparation of this substance will be detailed in the full account of this work.

(14) The structure of **15** was unambiguously established by transformation via conventional means into racemic $PGF_{2\alpha}$ methyl ester, mp 66–67 °C (lit.[15] 66.3–67.0 °C).

(15) Stork, G.; Isobe, M. *J. Am. Chem. Soc.* **1975**, *97*, 4745.

α-Chloro Boronic Esters from Homologation of Boronic Esters

Sir:

The potential value of α-haloalkaneboronic esters for carbon–carbon bond formation has been apparent since our first report of their behavior toward Grignard reagents,[1] and their utility for joining sterically hindered alkyl groups has been demonstrated elsewhere.[2] However, the various known routes to α-halo boronic esters[2-5] have lacked the generality and convenience needed for widespread synthetic utility.

(1) Matteson, D. S.; Mah, R. W. H. *J. Am. Chem. Soc.* **1963**, *85*, 2599–603.

(2) Brown, H. C.; De Lue, N. R.; Yamamoto, Y.; Maruyama, K. *J. Org. Chem.* **1977**, *42*, 3252–4. Brown, H. C.; De Lue, N. R.; Yamamoto, Y.; Maruyama, K.; Kasahara, T.; Murahashi, S.; Sonada, A. *Ibid.* **1977**, *42*, 4088–92.

(3) Matteson, D. S.; Liedtke, J. D. *Chem. Ind. (London)* **1963**, 1241. Matteson, D. S.; Schaumberg, G. D. *J. Org. Chem.* **1966**, *31*, 726–31. Matteson, D. S.; Cheng, T. C. *Ibid.* **1968**, *33*, 3055-3060.

(4) Matteson, D. S.; Arne, K. *J. Am. Chem. Soc.* **1978**, *100*, 1325–6.

(5) Rathke, M. W.; Chao, E.; Wu, G. *J. Organomet. Chem.* **1976**, *122*, 145–9.

0002-7863/80/1502-7588$01.00/0