Tetrahedron Letters,Vol.30,No.17,pp 2267-2268,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

CHIRAL INDUCTION IN A BIOMIMETIC OLEFIN CYCLIZATION

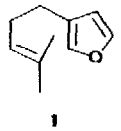
Hideyuki Takenaka,[1] Tomohiro Sato,[†] and Mugio Nishizawa[*]

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-Cho, Tokushima 770, Japan, [†]Shionogi Research Institute, Shionogi & Co. Ltd., Fukushimaku, Osaka 553, Japan

Abstract: Chiral induction has been achieved during a biomimetic cyclization of a chiral perillene derivatives in maximum 76% diastereomeric excess. The absolute configuration of the predominant products are established by X-ray diffraction study and chemical transformations.

Although a large number of studies have been carried out dealing with the biomimetic olefin cyclization into carbocycles, effective chiral induction is still a remaining problem in this field, though a few procedures have been reported.[2] We have developed an effective cyclization agent, mercury(II) triflate/amine complex,[3] and applied it to the synthesis of a variety of polycyclic terpenoids.[4,5] Herein described is an effective chiral induction (up to 76% de) during the cyclization of perillene derivatives with a variety of chiral acetals.

Chiral acetals **2a-2f** were prepared from perillene (**1**) via oxidation (SeO_2/*tert*-C_4H_9OOH/CH_2Cl_2) and subsequent acetalization with optically active tartaric acid derivatives according to Yamamoto's procedure.[6] When dimethyl tartarate derivative **2a** was treated with $Hg(OTf)_2$ (1.2 equiv)[7] in dichloromethane[8] at -78 °C for 4 h, a clean cyclization took place to give an organomer-



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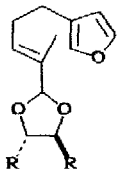
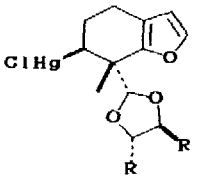
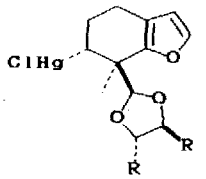


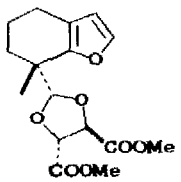
2a-f



3a-f



4a-f



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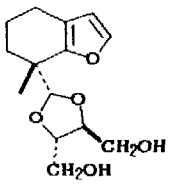

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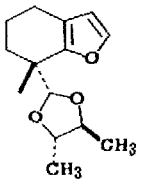

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a R = COOMe
b R = COOEt
c R = COO*i*-Pr
d R = COO*n*-Bu
e R = CH_3
f R = $CH_2OCH_2C_6H_5$

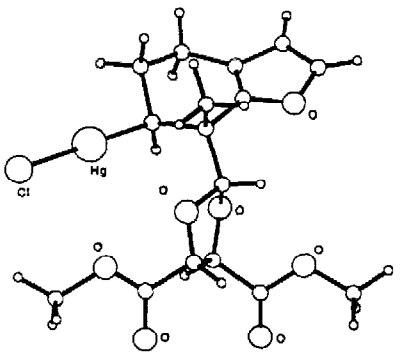
curic product in 44% yield after silica gel column chromatography along with the recovered starting material (36%). HPLC and NMR showed this product to be a 88:12 mixture of diastereoisomers **3a** and **4a**. These diastereomers were separated by preparative HPLC [YMC-D-SIL-5 column (4.6 x 250 mm), hexane and ethyl acetate (5:1)]. The resulting major isomer **3a** was crystallized from hexane and dichloromethane to give colorless needles, mp 112 °C, $[\alpha]_D^{20}$ +8.3° (*c* 2.37, $CHCl_3$).

The other tartarate derivatives **2b–2f** were also treated with $Hg(OTf)_2$ in dichloromethane under the same conditions as above to afford **3b–f** (major) and **4b–f** (minor), respectively, as summarized in Table 1. Alkyl tartarates **2a–2d** gave rather high diastereoface recognition during this cyclization than **2e** and **2f**, but chemical yields are better in the latter cases. The absolute configuration of the major products was established by the following ways. Single crystal X ray analysis revealed the absolute structure **3a**. In turn, **3a–3d** were converted into the identical dimethyl ester **5**, $[\alpha]_D^{21}$ -18.6° (*c* 1.22, $CHCl_3$), by reductive demercuration ($NaBH_4$/NaOH/C_2H_5OH/CH_2Cl_2) and re-esterification (CH_2N_2). A diol **6**, $[\alpha]_D^{19}$ -2.9° (*c* 1.26, $CHCl_3$), prepared by Li/NH_3 reduction of dibenzylether **3f**, was identical with a sample obtained by $LiAlH_4$ reduction of **5**. The diol **6** was tosylated (TsCl/Pyridine) and then reduced ($LiAlH_4$, reflux in dioxane). The resulting acetal **7**, $[\alpha]_D^{15}$ +13.5° (*c* 0.39, $CHCl_3$), was identified with that derived from **3e**.

Thus we have revealed that the chiral acetals originated from *L*-(+)-tartaric acid induce *R* configurations into the neighboring carbons within 16–76% diastereomeric excess during a biomimetic olefin cyclization.

Table 1. $Hg(OTf)_2$ induced cyclization of perillene derivatives.

olefin	**3**/**4** ratio	yield (%)
2a	88:12	44
2b	87:13	51
2c	85:15	46
2d	80:20	44
2e	70:30	53
2f	58:42	71



PLUTO Drawing of **3a**

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6. A. Mori, I. Arai, H. Yamamoto, H. Nakai, and Y. Arai, *Tetrahedron*, **1986**, *23*, 6447.
7. Acetals **2a–2f** did not react with $Hg(OTf)_2$/amine complex at all.
8. For the cyclization at low temperature, dichloromethane was found to be superior than nitromethane used commonly.
9. Crystal data of **3a**: $C_{16}H_{18}ClO_7Hg$, *M* 559.4, $P2_1$, *a* = 10.540(1), *b* = 14.575(2), *c* = 6.013(1) Å, β = 90.80(1)°, *V* = 923.7(2) Å^3, *Z* = 2. Final residual *R* 0.048 and R_w 0.058. Final atomic co-ordinates have been deposited at the Cambridge Crystallographic Data Centre.

(Received in Japan 1 March 1989)