Tetrahedron Letters,Vol.28,No.3,pp 311-314,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

3,4-EPOXY-5-HYDROXYCYCLOPENTENE VIA TITANIUM(IV)-CATALYZED PHOTOOXYGENATION AND ITS PYROLYSIS TO 2,4-PENTADIENOIC ACID.

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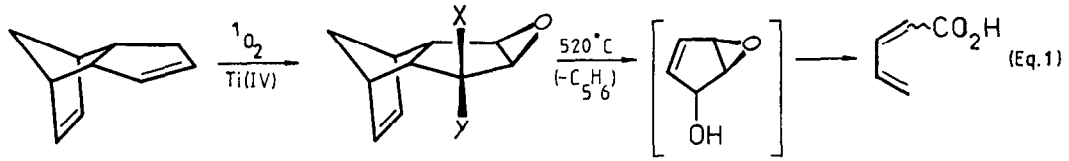
SUMMARY: The epoxy alcohol **exo**-6-hydroxy-**exo**-4-oxatetracyclo[6.2.1.0.^{2,7}0^{3,5}]-undec-9-ene (**1a**) was synthesized by photooxygenation of dicyclopentadiene in the presence of Ti(OiPr)$_4$; vacuum flash pyrolysis (520°C) of **1a** resulted in 3,4.epoxy-5-hydroxycyclopentene (**2**) as intermediate, which at elevated temperature rearranged into the **cis**- and **trans**-2,4-pentadienoic acids (**8**).

3,4-Epoxy-5-hydroxycyclopentene (**2**), a potentially valuable "Baustein" for the preparation of prostaglandin type products[1] in view of its high degree of functionality and three adjacent chirality centers, constitutes a challenging target molecule for organic synthesis. In view of our recent demonstration[2] that olefins with allylic hydrogen can be directly functionalized into hydroxy epoxides by photooxygenation in the presence of titanium (IV) alcoholate catalysts, the reaction sequence in Eq.1 offered an attractive route. Since the di-



1a (X=OH, Y=H)
1b (X=H, Y=OH)

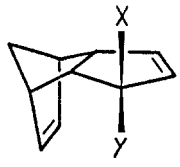
2

8

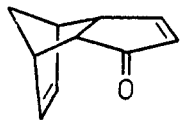
rect hydroxy-epoxidation proceeds under high enantiomeric control when the Ti(IV)-catalyzed photooxygenation is conducted in the presence of tartrate ester as chiral auxiliary[2], the sequence in Eq.1 would provide for the means of obtaining the hydroxy epoxide **2** in enantiomeric excess. Furthermore, the utilization of pyrolysis techniques, especially the cracking of dicyclopentadiene-derived substrates by the extrusion of cyclopentadiene, for the synthesis of sensitive products is well documented[3].

The photooxygenation of dicyclopentadiene in CH_2Cl_2 at 0 °C, using tetraphenylporphine (TPP) as sensitizer, gave the two hydroperoxides **3a,b** (95%) in

9:1 ratio (3a/3b).[4] Photooxygenation of dicyclopentadiene in the presence of



3a (X=OOH, Y=H)
3b (X=H, Y=OOH)
4a (X=OH, Y=H)
4b (X=H, Y=OH)



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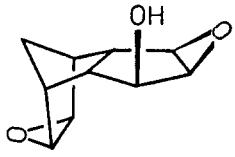

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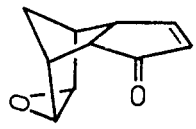

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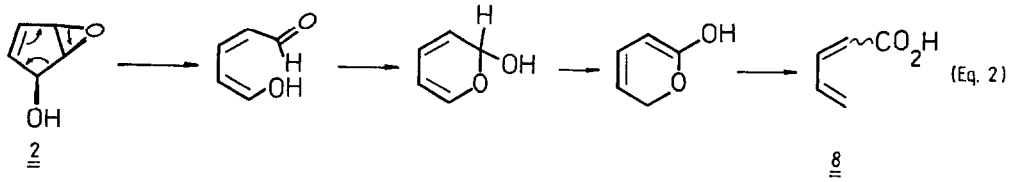
catalytic amounts (ca. 10%) of $Ti(OiPr)_4$ under the above conditions afforded indeed the expected **exo**-hydroxy epoxide **1a** in 70% yield (isolated by silica gel flash chromatography using CH_2Cl_2 as eluent). Our material matched the reported[5] physical and spectral data. In addition, the allylic alcohol **4a** (15%) and the diepoxide **6** (4%)[6] were isolated. Control experiments revealed that the pure **exo**-hydroperoxide **3a**[7] (obtained by silica gel chromatography eluting with CH_2Cl_2 and purified by Kugelrohr distillation, 80 °C at 0.1 Torr) gave on treatment with $Ti(OiPr)_4$ in CH_2Cl_2 at 0 °C **exo**-hydroxy epoxide **1a** (46%), alcohol **4a** (26%), dienone **5** (21%) and hydroxy diepoxyde **6** (7%). Sharpless epoxidation[8a] of the **exo**-alcohol **4a** with t-butylhydroperoxide and $VO(acac)_2$ as catalyst, gave quantitatively the **exo**-epoxy alcohol **1a** (>90%) after Kugelrohr distillation (78-80 °C at 0.1 Torr). However, under similar Sharpless conditions[8b] the **endo**-alcohol **4b** gave a mixture of the dienone **5** (48%) and the epoxy enone **7**[9] (52%), but no **endo**-hydroxy epoxide **1b**. Steric reasons must be responsible for the failure of transforming **4b** or **3b** into **1b** in the Ti(IV)- or V(V)-mediated oxygen transfers.

The pyrolysis of the hydroxy epoxide **1a** by subliming (75-80 °C at 0.1 Torr) the substrate through a 60-cm long quartz tube required a minimum of ca. 520 °C. Condensation of the effluent from the above pyrolysis into a dry ice trap afforded a 1:1 mixture of the (E)- and (Z)-2,4-pentadienoic acids (**8**) in 50% yield (Eq. 1).[10] Clearly, these pyrolysis temperatures were too high for the desired 3,4-epoxy-5-hydroxycyclopentene (**2**) to survive.

The mechanistic scheme in Eq. 2 offers a rational explanation for the



(Eq. 2)

2 **8**

formation of the dienic acids **8**, suggesting that the hydroxy epoxide **2** figured as intermediate in the interesting transformation **1a**→**8** (Eq. 1). It has been reported[11] that 2,3-epoxycyclopenten-1-one gave on pyrolysis α-pyrone via a sequence analogous to the first two steps in Eq. 2. However, in the present case a facile 1,5-hydrogen shift and subsequent electrocyclic reversion gene-

rates the 2,4-pentadienoic acids **8** as final product.

To realize our goal of preparing the 3,4-epoxy-5-hydroxycyclopentene (**2**) via the convenient synthetic sequence will require finding precursors wich pyrolyze at more moderate temperatures (<200 °C). For this purpose [2+2] photoadducts of cyclopentadiene and anthracene derivatives are being presently explored as viable precursors.

ACKNOWLEDGEMENTS

We are grateful to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and the Italian Consiglio Nazionale delle Ricerche for generous support and thank Dr. G. Lange (MS) and Dr. D. Scheutzow (NMR) for spectral services and B. Will for technical assistance.

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6. exo-6-Hydroxy-exo-4-exo-10-dioxapentacyclo[6.3.1.0.^{2,7}0.^{3,5}0^{9,11}]dodecane (**6**), m.p. 128-130 °C (CH_2Cl_2/Et_2O), colorless powder.- IR (KBr): 3480, 3060, 3020, 2980, 1460, 1390, 1340, 1235, 1080, 860, 825, 730 cm^{-1}.- ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.79 (br.d, $J_{12s,12a}$ = 9.9 Hz; 1H, 12a-H), 1.45 (ddd, $J_{12s,12a}$ = 9.9 Hz, $J_{1,12s}$ = $J_{8,12s}$ = 1.8 Hz; 1H, 12s-H), 2.17 (ddd, $J_{2,7}$ = 8.4 Hz, $J_{1,2}$ = 4.5 Hz, $J_{1,12}$ = 1.8 Hz; 1H, 2-H), 2.67 (m; 1H, 2-H), 2.77 (m; 1H, 8-H), 2.79 (dd, $J_{2,7}$ = 8.4 Hz, $J_{7,8}$ = 4.4 Hz; 1H, 7-H), 3.21 (d, $J_{9,11}$ = 3.0 Hz; 1H, 11-H), 3.25 (d, $J_{9,11}$ = 3.0 Hz; 1H, 9-H), 3.54 (d, $J_{5,6}$ = 2.3 Hz; 1H, 6-H), 3.68 (dd, $J_{3,5}$ = $J_{5,6}$ = 2.3 Hz; 1H, 5-H), 4.32 (dd, $J_{3,5}$ = 2.3 Hz, $J_{2,3}$ = 2.2 Hz; 1H, 3-H).- ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 28.71 (t; C-12), 38.87 (d), 39.27 (d), 47.76 (d), 48.36 (d), 48.58 (d), 54.01 (d), 60.56 (d), 63.51 (d), 71.06 (d).- MS (70 eV): m/e = 180 (0.3%; M$^+$), 179 (1%), 161 (2%), 149 (7%), 133 (10%), 123 (28%), 111 (15%), 105 (24%), 98 (100%), 91 (49%), 81 (88%), 79 (67%), 77 (59%), 71 (26%), 55 (47%), 41 (46%).- $C_{10}H_{12}O_3$ (180.2) Calcd. C 66.65, H 6.71; Found C 66.69, H 6.84.
7. exo-5-Hydroperoxytricyclo[5.2.1.0^{2,6}]deca-3,8-diene (**3a**) b.p. 80°C at 0.1 Torr.- IR (CCl_4): 3650, 3600-3200 (broad), 3140, 3040, 2960, 2930, 1750, 1480, 1360, 1120, 1040, 1000, 980, 930, 870 cm^{-1}.- ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.42 (br.d, $J_{10s,10a}$ = 8.1 Hz; 1H, 10a-H), 1.58 (ddd, $J_{10s,10a}$ = 8.1 Hz,

$J_{1,10s}$ = $J_{7,10s}$ = 1.7 Hz; 1H, 10s-H), 2.72 (ddd, $J_{2,6}$ = 7.5 Hz, $J_{1,2}$ = 4.5 Hz, $J_{2,3}$ = 2.2 Hz; 1H, 2-H), 2.83 (m; 1H, 7-H), 3.03 (m; 1H, 1-H), 3.36 (m; 1H, 6-H), 4.45 (m; 1H, 5-H), 5.60 (dt, $J_{3,4}$ = 5.7 Hz, $J_{3,4}$ = 1.8 Hz, $J_{4,6}$ = 1.2 Hz; 1H, 4-H), 5.84 (dd, $J_{8,9}$ = 5.7 Hz, $J_{7,8}$ = 3.0 Hz; 1H, 8-H), 5.93 (br.d, $J_{3,4}$ = 5.7 Hz, $J_{3,6}$ = 1.0 Hz; 1H, 3-H), 5.96 (dd, $J_{8,9}$ = 5.7 Hz, $J_{1,9}$ = 3.0 Hz; 1H, 9-H), 8.93 (br.s; 1H, OOH).- ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 44.42 (d), 44.61 (d), 47.88 (d), 51.04 (t; C-10), 54.25 (d), 92.74 (d), 129.38 (d), 132.19 (d), 135.38 (d), 141.54 (d).- MS (70 eV): m/e = 164 (0.3%; M^+), 146 (16%), 130 (8%), 117 (26%), 115 (14%), 91 (23%), 82 (66%), 77 (17%), 66 (100%, $C_5H_6^+$), 55 (10%), 51 (16%).-

$C_{10}H_{12}O_2$ (164.2): Calcd. C 73.15, H 7.37; Found C 72.90, H 7.16

8.a) A solution of 5.00 g of the alcohol **4a** in 50 ml of dry CH_2Cl_2 and 2.5 mol% $VO(acac)_2$ was treated at 0°C with 12 ml (1.1 eq.) 3.0 M tBuOOH in CH_2Cl_2 and refluxed overnight. After roto-evaporation (ca. 20°C at 10-20 Torr) of the solvent the product was purified by Kugelrohr distillation.

b) Run as above, except the products **5** and **7** were separated by silica gel chromatography using 8:2 CH_2Cl_2/petroleum ether (30-50) as eluent.

9. exo-9-Oxatetracyclo[5.3.1.0.^{2,6}0^{8,10}]undeca-3-en-5-one (7): colorless prism, m.p. 150-151°C (CH_2Cl_2/Et_2O).- IR (KBr): 2980, 1700, 1350, 1320, 1230, 1215, 1180, 1090, 1060, 1020, 1000, 970, 920, 880, 850, 810, 770, 690 cm^{-1}.- ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.07 (br.d, $J_{11s,11a}$ = 10 Hz; 1H, 11a-H), 1.56 (br.d, $J_{11s,11a}$ = 10.0 Hz; 1H, 11s-H), 2.65 (m; 2H), 2.79 (m; 2H), 3.04 (d, $J_{8,10}$ = 3.1 Hz; 1H, 8-H or 9-H), 3.34 (m; 1H, 6-H), 6.06 (dd, $J_{3,4}$ = 5.9 Hz, $J_{2,4}$ = 1.7 Hz; 1H, 4-H), 7.51 (dd, $J_{3,4}$ =5.9 Hz, $J_{2,3}$ = 2.6 Hz; 1H, 3-H).- ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 30.33 (t; C-11), 37.35 (d), 38.63 (d), 40.30 (d), 48.76 (d), 49.87 (d), 51.10 (d), 136.75 (d; C-4), 162.91 (d; C-3), 208.86 (s; C=O).- MS (70 eV): m/e = 163 (3%, M^++1), 162 (22%, M^+), 161 (4%), 133 (13%), 105 (14%), 91 (13%), 82 (65%), 81 (100%), 79 (13%), 78 (23%), 77 (19%), 66 (15%), 55 (15%).-

$C_{10}H_{10}O_2$ (162.09): Calcd. C 74.04, H 6.22; Found C 74.16, H 6.39.

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(Received in Germany 17 October 1986)