Non-Hazardous Preparation of 3-Acetoxy- and 3-Oxodicyclopentadienes

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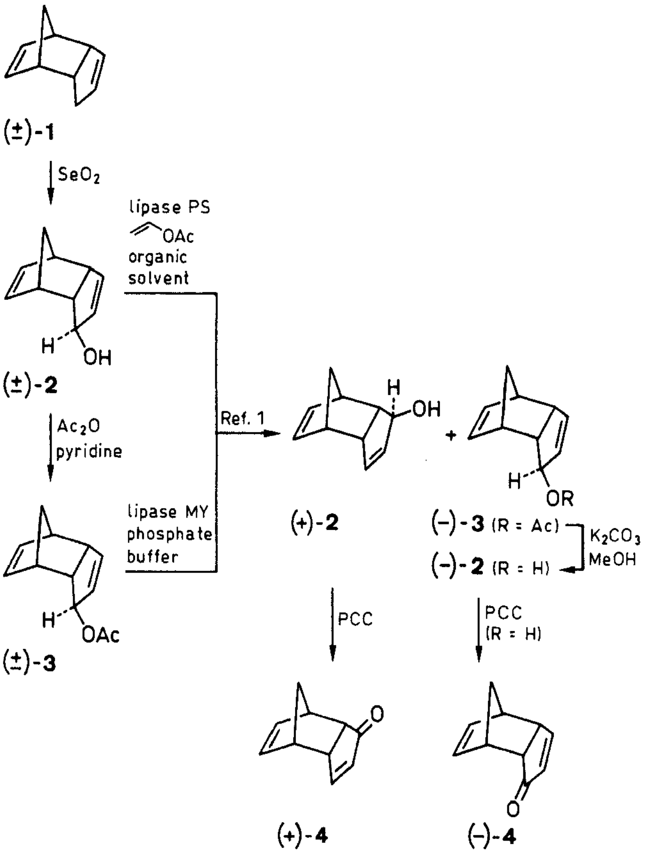
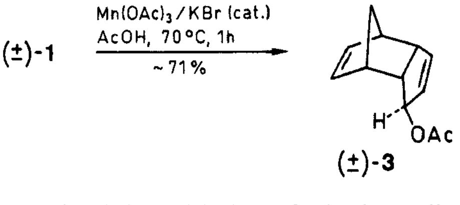
Acetoxy- and oxodicyclopentadienes were prepared efficiently using non-hazardous oxidants in place of the conventional toxic reagents.

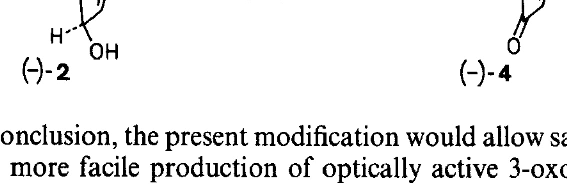
Racemic 3-hydroxydicyclopentadiene (**2**) and its acetate **3** are suitable substrates for the lipase-mediated kinetic resolution[1] to produce optically pure **2** and **3**. When the former was treated with vinyl acetate in an organic solvent in the presence of lipase PS (Amano),[1b] (+)-alcohol (+)-**2** and (−)-acetate (−)-**3** are generated in high optical yields, similarly the latter also furnished the same alcohol (+)-**2** and the same acetate (−)-**3** under the hydrolytic conditions in a phosphate buffer solution in the presence of lipase MY (Meito).[1a] Both the optically active materials are precursors of optically active 3-oxodicyclopentadiene (**4**) which has found versatile use as a powerful chiral building block in the enantiocontrolled synthesis of a variety of natural products.[1b,2,3] The most convenient preparation of the racemic precursors so far reported employs selenium dioxide oxidation[4] of dicyclopentadiene (**1**) which allows introduction of the oxygen functionality at the requisite position. Moreover, the optically active alcohol **2**, after resolution, requires a chromate oxidant[1a] to convert it into optically active 3-oxodicyclopentadiene (**4**). Since these approaches are considerably restricted by toxicity of the oxidants used, we explored alternative procedures replacing these conventional reagents and herein we wish to report a modification involving one-step preparation of the racemic acetate (±)-**3** from dicyclopentadiene [(±)-**1**] and oxidation of optically active 3-hydroxydicyclopentadiene [(+)-**2**] to optically active 3-oxodicyclopentadiene [(+)-**4**] without using hazardous oxidizing agents.



We first examined the oxidation of dicyclopentadiene [(±)-**1**] using manganese(III) acetate in the presence of potassium bromide which has been reported to accelerate the rate of oxidation of olefins into the corresponding allylic acetates.[5] As expected when (±)-**1** was treated with manganese(III) acetate,[5] prepared in situ, in a warm mixture of acetic acid and acetic anhydride in the presence of potassium bromide *exo*-acetoxydicyclopentadiene [(±)-**3**] was generated in a stereospecific manner. Thus, in a small scale preparation using 36 mmol of (±)-**1**, 71 % yield of the *exo*-acetate [(±)-**3**] was obtained after purification by column chromatography and in a large scale preparation using 0.3 mole of (±)-**1**, 50 % yield of (±)-**3** was obtained by vacuum distillation. The present procedure may be compatible in yield with the conventional one using selenium dioxide which produces 3-hydroxydicyclopentadiene [(±)-**2**] in 57 % yield after distillation in 0.6 molar scale experiment.



We next examined the oxidation of 3-hydroxydicyclopentadiene (**2**) into 3-oxodicyclopentadiene (**4**) without using the conventional chromate oxidants, such as pyridinium chlorochromate. Among the reagents tried, manganese(IV) dioxide[6] gave the best result. Thus, when the optically pure alcohol (+)-**2**, obtained via the lipase-mediated kinetic resolution, was stirred with an excess of manganese(IV) oxide in warm dichloromethane, a clean reaction occurred to give (+)-3-oxodicyclopentadiene [(+)-**4**] in nearly quantitative yield without loss of the original chiral integrity.



In conclusion, the present modification would allow safer and more facile production of optically active 3-oxodicyclopentadiene (**4**) and expand versatile utility of **4** as a chiral building block.

Melting points are uncorrected. IR spectra were recorded on a JASCO-IR-700 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-3000 (300 MHz). Mass spectra were measured on a

JEOL JMS-DX303 instrument. Optical purities were determined on a Gilson Model-307 instrument equipped with a chiral column. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter. Chemical reactions were carried out under Ar.

***exo*-3-Acetoxydicyclopentadiene (*exo*-3-acetoxytricyclo[5.2.1.0^{2,6}]-deca-4,8-dien-3-one) [±)-3]:**

(a) Small Scale Reaction: To a solution of $Mn(OAc)_2 \cdot 4H_2O$ (10.0 g, 40.8 mmol) in AcOH (40 mL) was added Ac_2O (15 mL) and the mixture was refluxed for 20 min. To this hot solution (~ 110 °C) was added portionwise $KMnO_4$ (1.61 g, 10.2 mmol) and the mixture was refluxed for 30 min. After cooling to 70 °C, dicyclopentadiene (4.9 mL, 36 mmol) was added followed by KBr (730 mg, 6.2 mmol) with stirring and the stirring was continued at the same temperature until the dark brown color of Mn(IV) ion had faded (~ 1 h). After cooling, the mixture was filtered through a Celite pad, diluted with H_2O and extracted with hexane. The extract was washed successively with 5% aq $NaHCO_3$, H_2O, brine, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on a silica gel column (100 g, Et_2O/hexane, 1:20) to afford the acetate (±)-**3** as a colorless oil; yield: 3.43 g (71%).

IR (neat): $\nu = 1732\ cm^{-1}$.

^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.06$ (1 H, dd, $J = 5.4$, 2.4 Hz), 5.84–5.89 (1 H, m), 5.83 (1 H, dd, $J = 5.4$, 2.4 Hz), 5.55 (1 H, dt, $J = 5.9$, 1.8 Hz), 4.92–4.95 (1 H, m), 3.33–3.40 (1 H, m), 3.88 (1 H, br s), 2.80 (1 H, br s), 2.57 (1 H, dq, $J = 6.9$, 2.2 Hz), 2.01 (3 H, s), 1.57 (1 H, d, $J = 8.4$ Hz), 1.38 (1 H, d, $J = 8.4$ Hz).

MS: $m/z = 190$ (M^+), 66 (100%).

HRMS: m/z calc. for $C_{12}H_{14}O$ 190.0993, found 190.1009.

Spectral data and chomatographical behavior were identical with those of an authentic material.[1]

(b) Large Scale Reaction: To a solution of $Mn(OAc)_2 \cdot 4H_2O$ (100 g, 0.408 mol) in AcOH (300 mL) was added Ac_2O (154 mL) and the mixture was refluxed for 20 min. To this hot solution (~ 110 °C) was added portionwise $KMnO_4$ (16.12 g, 0.102 mmol) and the mixture was refluxed for 30 min. After cooling to 70 °C, dicyclopentadiene (43.7 mL, 0.326 mol) was added to this mixture followed by KBr (4.86 g, 40.8 mmol) with stirring at the same temperature until the dark brown color of Mn(IV) ion had faded (~ 1 h). After cooling, the mixture was filtered through a Celite pad, diluted with H_2O and extracted with hexane. The extract was washed successively with 5% aq $NaHCO_3$, H_2O, brine, dried ($MgSO_4$), and evaporated under reduced pressure to leave a brown oil which was distilled under vacuum to give the acetate (±)-**3** as a colorless oil; yield: 24.2 g (50%); bp 66–69 °C/0.04 Torr. Spectral data and chromatographic behavior were identical with those of an authentic material (see above).

Conversion of (+)-*exo*-3-Hydroxydicyclopentadiene [(+)-(1*R*,2*R*,3*S*,6*R*,7*S*)-3-hydroxytricyclo[5.2.1.0^{2,6}]deca-4,8-diene] [(+)-2] into (+)-3-Oxodicyclopentadiene [(+)-(1*R*,2*R*,6*R*,7*S*)-Tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one [(+)-4]:

A suspension of (+)-**2** ($[\alpha]_D^{28}$ +97.5° ($c = 1.09$, $CHCl_3$), mp 71.5–72.0 °C, > 99% ee by HPLC: Chiralcel OB, *i*-PrOH/hexane, 1:9) (2.01 g, 13.6 mmol) and MnO_2 (10.0 g, 115 mmol) in CH_2Cl_2 (20 mL) was stirred at 38 °C (bath temperature) for 24 h. After cooling the mixture was filtered through a Celite pad and evaporated under reduced pressure to leave the ketone (+)-**4** as a colorless crystalline solid which was pure for practical use; yield: 1.92 g (97%). This was purified by chromatography on a silica gel column (50 g, EtOAc/hexane, 1:10) to leave pure (+)-**4** as colorless plates; yield: 1.87 g (94%), mp 76.0 °C, $[\alpha]_D^{28}$ +139.5° ($c = 0.94$, MeOH) [Lit.[1] mp 76.5–77.0 °C; $[\alpha]_D^{25}$ +140.3° ($c = 0.95$, MeOH)], > 99% ee by HPLC (Chiralcel OB, *i*-PrOH/hexane, 1:9).

IR (neat): $\nu = 1690\ cm^{-1}$.

^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$ (1 H, dd, $J = 5.5$, 2.2 Hz), 5.95 (1 H, dd, $J = 5.5$, 1.6 Hz), 5.93 (1 H, dd, $J = 5.5$, 2.9 Hz), 5.77 (1 H, dd, $J = 5.5$, 2.9 Hz), 3.38–3.44 (1 H, m), 3.40 (1 H, br s), 2.96 (1 H, br s), 2.79 (1 H, t, $J = 5.1$ Hz), 1.74 (1 H, t, $J = 8.4$ Hz), 1.61 (1 H, d, $J = 8.4$ Hz).

MS: $m/z = 146$ (M^+), 66 (100%).

HRMS: m/z calc. for $C_{10}H_{10}O$ 146.0731, found 146.0733.

Spectral data and chromatographical behavior were identical with those of an authentic material.

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