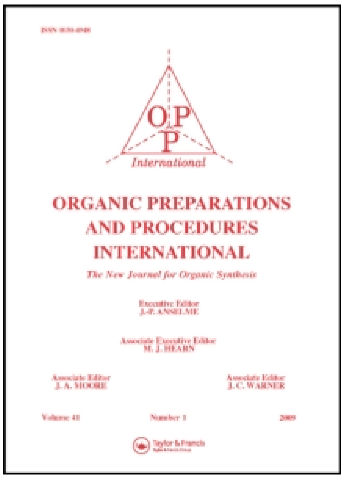

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SYNTHESIS OF *cis*-Δ^6-OCTALIN-1,4-DIONE *bis*-ACETALS

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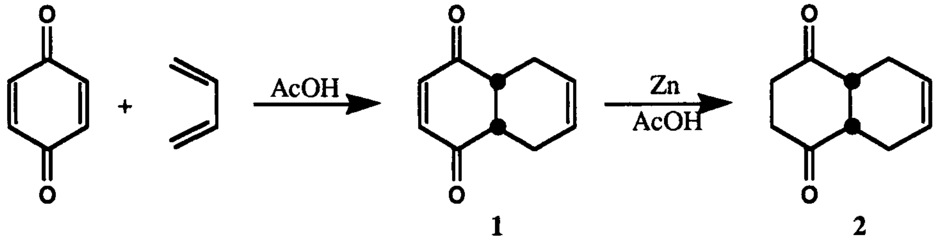
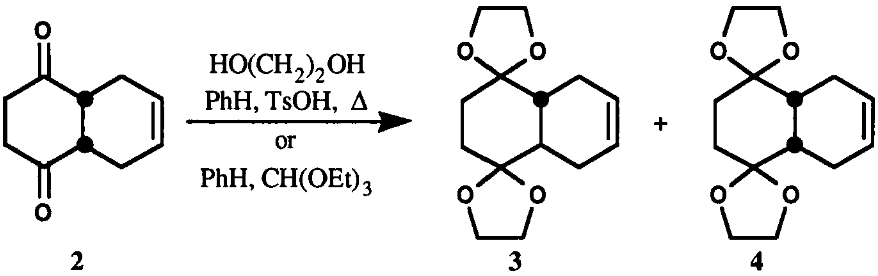
cis-Fused decalins are present in a variety of natural products including sesquiterpenes,[1] and have been used as precursors to steroids.[2] One convenient source of the *cis*-fused decalin ring system which contains suitable functionality for further elaboration is the Diels-Alder adduct 1 derived from *p*-benzoquinone and butadiene. Reduction of 1 with Zn/AcOH affords *cis*-dione 2 (Eq. 1).[3] Unfortunately, as Marshall and Ireland discovered,[2] bisacetalization under standard conditions leads exclusively to the *trans*-fused bisacetal 3 (Eq. 2).[4] We felt that one of the milder methods of acetal formation might give rise to the desired *cis*-fused system. However, reaction of 2 at room temperature with ethylene glycol and $HC(OMe)_3$ afforded only 9:1 mixture of *trans* and *cis* bisacetals 3 and 4, respectively (Eq. 2).

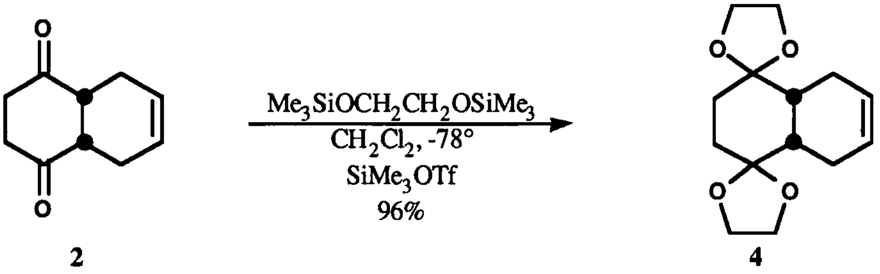


(1)



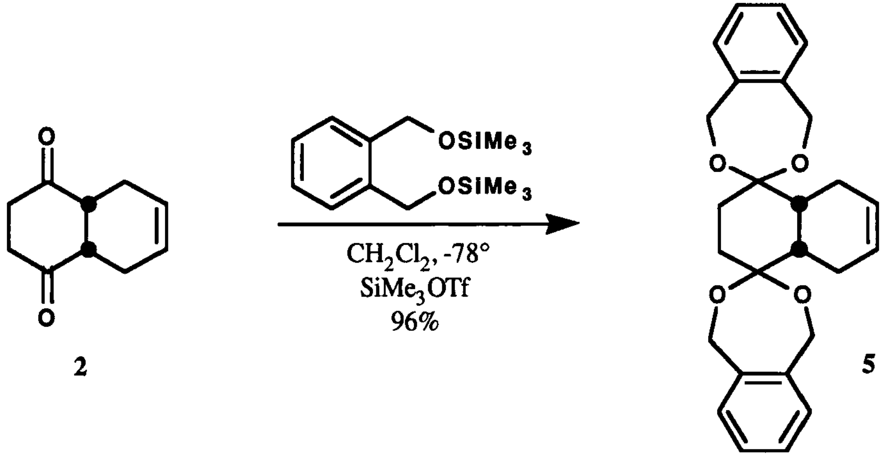
(2)

Recently, Noyori has demonstrated the superiority of an aprotic acetalization procedure in some cases where double bond migration may occur during acetal formation. This procedure is



(3)

very mild and the reaction occurs somewhere between -78 and -20°.[5] Application of Noyori's procedure for the protection of dione **2** led to the exclusive formation of the desired *cis*-fused bisacetal **4** in 96% yield (Eq. 3). No formation of the *trans*-bisacetal **3** was evident by ^{1}H NMR analysis of the crude product. Mori has exploited this aprotic acetalization methodology for the formation of *o*-xylylene–α,α'-dioxy protected ketones, the advantage of this protecting group being its facile cleavage by catalytic hydrogenation to restore the ketone functionality.[6] Dione **2** could likewise be protected as its bis-*o*-xylylene–α,α'-dioxy derivative **5** in 70% yield (Eq. 4). We believe that compound **5** contains the *cis*-fused decalin ring system; however, since the *trans*-fused compound is unknown we were unable to make a direct comparison.



(4)

EXPERIMENTAL SECTION

^{1}H NMR Spectra (200 MHz) were determined on a Magnachem instrument, ^{1}H NMR spectra (300 MHz) and ^{13}C NMR (75.6 MHz) spectra were obtained on a GN-300 spectrometer. All NMR spectra were recorded in $CDCl_3$ unless otherwise noted. Chemical shifts are given in ppm relative to TMS (0 ppm, ^{1}H) and $CDCl_3$ (77.0 ppm, ^{13}C). ^{1}H NMR coupling constants (J) are given in Hz. IR spectra were obtained on a Perkin-Elmer infrared spectrometer. Melting points are uncorrected. Mass spectra were obtained on MAT CH-5-DF (FAB), and Finnigan 8230 B (EI) mass spectrometers. Elemental analyses were performed by The Upjohn Company. The following chemicals were obtained from commercial sources and were used without further purification: 80% *m*-CPBA, *N*-benzylidenebenzenesulfonamide, trimethylsilyl trifluoromethanesulfonate (triflate) (Aldrich), 1,2-bis(trimethylsiloxymethyl)benzene, 1,2-bis(trimethylsiloxy)ethane (Fluka). Methylene chloride was distilled from CaH_2 just prior to use. All reactions were carried out in oven-dried glassware under a N_2 atmosphere. *cis*–Δ^6-Octalin-1,4-dione **2**, was prepared according to the literature procedure.[3]

***cis*-Δ^6-Octalin-1,4-dione bis-Ethylene Acetal (4).**- This compound was prepared by a slight modification of the Noyori procedure[5] for aprotic acetalizations. To a stirred solution of trimethylsilyl triflate (45 µl, 0.27 mmol) in 75 mL of CH_2Cl_2 at -78° was added 1,2-bis(trimethylsiloxy)ethane (7.37 mL, 30.1 mmol) under a nitrogen atmosphere. A solution of *cis*–Δ^6-octalin-1,4-dione (**2**) (2.25 g, 13.7 mmol) in CH_2Cl_2 (25 mL) was then added, and the mixture was stirred at -78° for 6.5 hrs and at -22° for 18 hrs. Isolation by extractive purification as described by Noyori gave 3.33 g (96%) of **4** as a white solid. Although this material was sufficiently pure for most applications, it could be further purified by crystallization from hexanes, mp. 116° (needles); ^{1}H NMR (300 MHz): δ 1.51 (m, 2H), 1.73 (m, 2H), 1.92 (m, 2H), 2.07 (m, 4H), 3.79 (m, 8H, $OC\underline{H}_2$), 5.48 (s, 2H, $C = C\underline{H}$); ^{13}C NMR (75.6 MHz): δ 23.88, 29.99, 38.68, 63.81, 64.67, 109.96, 125.14; MS (EI): m/z at 252 (M^+).

Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.50; H, 7.93

***trans*-Δ^6-Octalin-1,4-dione bisEthylene Acetal (3).**- To enable an NMR comparison, this compound was prepared as described previously,[2] mp. 95° (hexanes); ^{1}H NMR (200 MHz): δ 1.75 (s, 4H), 2.05 (s, 6H), 3.95 (s, 8H, $OC\underline{H}_2$), 5.63 (s, 2H, $C = C\underline{H}$).

bisAcetal 5.- According to the procedure described for the synthesis of bisacetal **4**, *cis*–Δ^6-octalin-1,4-dione (**2**) (200 mg, 1.22 mmol) and 1,2-bis-(trimethylsiloxymethyl)benzene (756 mg, 2.68 mmol) were treated with trimethylsilyl triflate (4.0 μL, 0.024 mmol) to give 647 mg of a white solid. Recrystallization of the crude solid from ether gave 344 mg (70%) of **5** as a white solid, mp. 194-196°; ^{1}H NMR (200 MHz): δ 1.92 (m, 2H), 2.12 (m, 4H), 2.49 (m, 4H), 4.57 (d, J = 15, 2H, $2OC\underline{H}$), 4.77 (d, J = 15, 2H, $2OC\underline{H}$), 5.14 (d, J = 15, 2H, $2OC\underline{H}$), 5.14 (d, J = 15, 2H, $2OC\underline{H}$), 5.75 (s, 2H, $C = C\underline{H}$), 7.16 (m, 8H, ArH); MS (EI): m/z at 404 (M^+).

Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.20; H, 6.98. Found: C, 76.90; H, 6.80

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