STEREOSELECTIVE SYNTHESIS OF 1,2-DIETHOXY- AND 1,4-DIOXINO[2,3-b]FURANS USING ORGANOIRON REAGENTS

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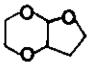
Dedicated to Professor Gilbert Stork on the occasion of his 65th birthday.

Abstract —— Use of the readily available organoiron complexes 3 and 13 for the stereoselective synthesis of 2,3-dialkoxytetrahydrofurans is reported. The novel tricyclic dioxinofuran 17 can be prepared from complex 13a, while 13b yields the related, optically active 20 ([α]$_D^{20}$ = +57.04°), with defined absolute configuration at 6-centers.

The 2,3(1,4-dioxino)-furan heterocyclic system 1, which is formally equivalent to the acyclic α,γ-dihydroxyaldehyde 2, is comparatively uncommon among heterocyclic systems.



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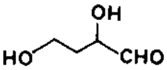

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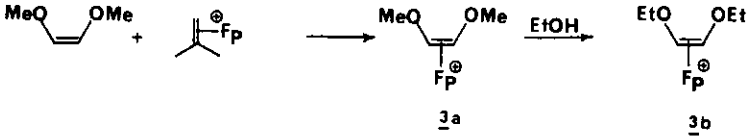
A limited number of these substances have been prepared from o-quinones and furans through either photochemically[1] or thermally[2] initiated (2+4) cycloaddition reactions, but these reactions are often complicated by the concurrent formation of oxetanes. Gluco- and xylofuranoses have also been converted to dioxinofurans through either intramolecular etherification of 1-chloroethyl-D-glucofuranosides[3] or intramolecular glycosidation of 2-O-hydroxyalkyl derivatives,[4] and a few gluco- and xylofuranoses have been transformed to 1,2′:2,1′-dianhydrides which incorporate the dioxinofuran system.[5] Finally, this heterocyclic system finds brief mention in the literature as a product of the rearrangement of a dioxane fused cyclopropanecarboxylic acid[6] and as a tricyclic system incorporating an α-pyridone ring.[7]

Herein, we wish to report the use of the readily available iron complexes 3 and 13 for the stereoselective preparation of 2,3-alkoxyfurans, including two tricyclic dioxinofurans. The procedures outlined should serve as a general preparative route to these compounds.

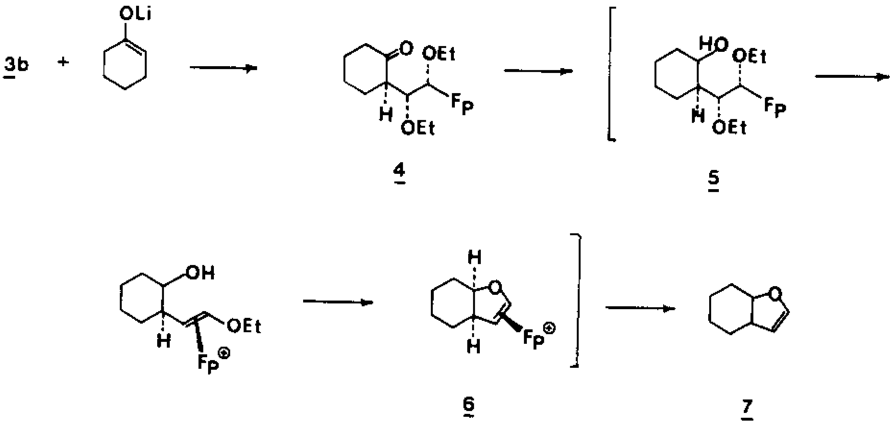
Complex 3a is readily available in multigram quantities by exchange complexation[8] of cis-1,2-dimethoxyethylene[9] with Fp(isobutylene)BF$_4$.[10] (The symbol Fp is used here for the C$_5$H$_5$Fe(CO)$_2$

group). This salt is transformed to the diethoxy analog in essentially quantitative yield by brief slurrying in ethanol at room temperature followed by the addition of ether to reprecipitate the salt 3b.[11]



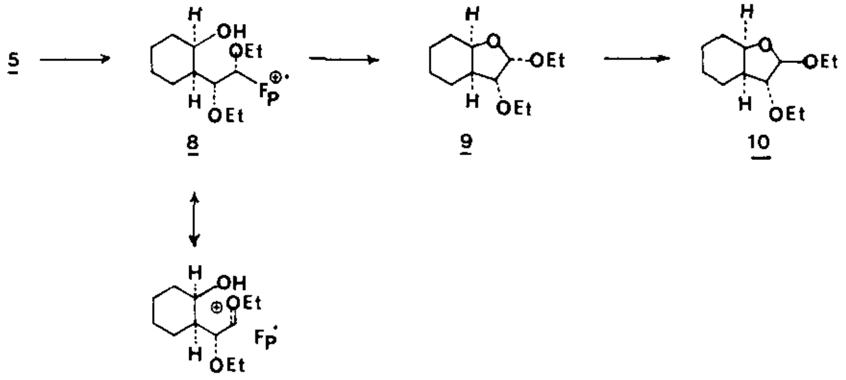
Lithium cyclohexanone enolate reacted cleanly with 3b at -78 °C in THF solution to give the neutral adduct 4 as a *single diastereomer* (96%). Reduction of this adduct with L-Selectride gave the hydroxy diether 5 as a 10:1 mixture of diastereomers in high yield. Attempted purification of this product on alumina led to extensive decomposition and the formation of the hexahydrobenzofuran 7 as the major product.

We have previously reported the transformation of 4 by acid treatment to complex 6[11] and it seems likely that the formation of 7 proceeds similarly by Lewis acid promotion on the alumina surface and subsequent loss of the Fp group:

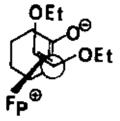


Oxidation of unpurified 5 with ceric ammonium nitrate in THF solution proceeded with loss of the Fp group to give, unexpectedly, the tetrahydrofuran 9. The *cis*-configuration of the ethoxy groups in this product was established by NOE experiments and confirmed by epimerization of the acetal center in the presence of HCl in ethanol to the more stable *trans* isomer 10. The epimerization is evidenced by a change in chemical shift and coupling constant for the acetal proton (9 δ 5.01, J=5.4 Hz; 10 δ 4.98, J=3.6 Hz), which is in accord with observations made for *cis*- and *trans*-dimethoxydihydrobenzofuran.[12]

The exclusive formation of the *cis* isomer suggests that oxidation of the iron center, to give cation radical 8, is followed by rapid displacement of the Fp group as the relatively stable Fp radical, possibly by a concerted mechanism. The presence of the α-ethoxy group in 5 must however play a significant role in stabilizing the incipient carbonium ion and is no doubt responsible for diverting intermediate 8 from the anticipated course of reaction of carbonyl insertion. Cutler and coworkers[13] have previously observed that (α-alkoxyalkyl)Fp complexes are relatively resistant to carbonyl insertion reactions.



The cis,trans,cis structure, depicted for 9, is supported by NOE experiments and is compatible with a transition state for the condensation reaction of 3b with cyclohexanone enolate involving a gauche arrangement of donor and acceptor components, with the smallest substituent of the donor molecule antiperiplanar to the acceptor olefin center,[14,15] as shown in structure 11. The diastereomeric arrangement of these components, 12, may be disfavored by steric interactions between an ethoxy group in the acceptor complex and the C-4 axial hydrogen in the donor.



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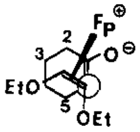


12

Brief treatment of 3a with ethylene glycol at 0 °C leads to exchange etherification and the quantitative formation of the dihydrodioxin complex 13a.

13 a

When this salt is treated with lithium cyclohexanone enolate at -78 °C the adduct, 14, is formed in 96% yield as a single diastereomer. The structure of this substance was determined by single crystal x-ray analysis. Slow evaporation of a petroleum ether solution of 14 at -20 °C provided crystals suitable for the x-ray study. The compound crystallized in the monoclinic space group $P2_1/c$ with a = 12.857, b = 7.708, c = 17.960 Å and β = 108.468°. Additional structural information is given in Tables I and II, and an ORTEP plot of the molecular structure, with the important atoms labelled, is shown in Figure 1.

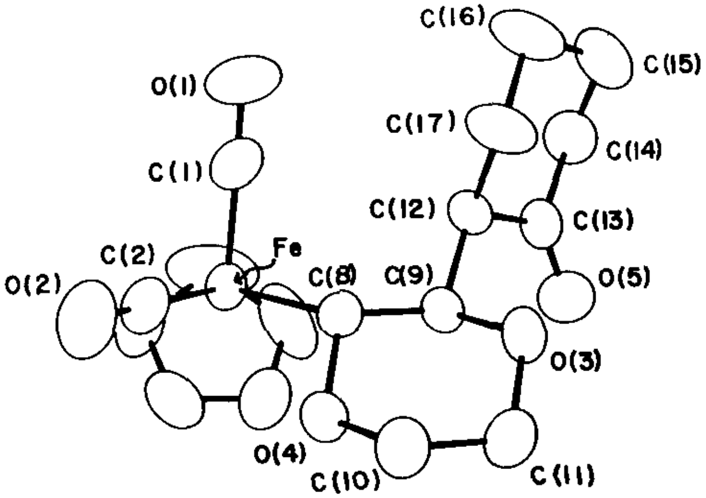
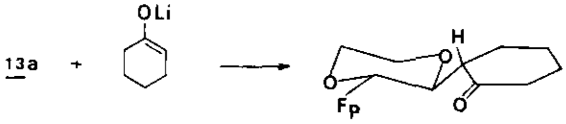


Figure 1. A perspective view of compound 14. (ORTEP plot showing 50% probability ellipsoids. For labeling of Cp carbon atoms, C(3) lies behind C(2) and others continue clockwise).

The relative configurations of the three adjacent chiral centers in 14 are, like those in 4, compatible with a gauche orientation of the reacting components in the transition state in which the dioxino ring is oriented so as to avoid interaction with the axial hydrogen at C-4 of the enolate. This is shown in structure 15a.



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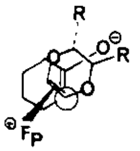
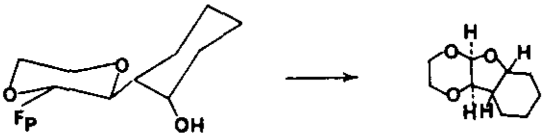


a R = H

b R = Me

15

Reduction of 14 with L-Selectride gave the alcohol 16, which was then oxidized with ceric ammonium nitrate. Like 5 this reaction proceeded with demetallation and ring closure, and gave the tricyclic dioxinofuran 17. NOE experiments supported the cis-anti-cis configuration for this compound. As anticipated, treatment of 17 with dry HCl in THF failed to epimerize the acetal center.



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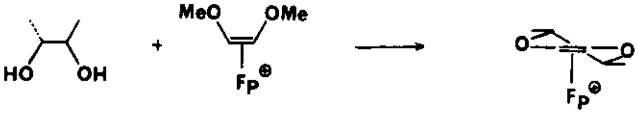
Finally, these transformations may be carried out enantioselectively by the use of the optically active dihydrodioxin iron complex 13b, prepared by exchange etherification of 3a with (R,R)-2,3-butanediol.



13b

This substance has been shown to add a variety of carbon and heteroatomic nucleophiles regiospecifically.[16] With lithium cyclohexanone enolate, the single product 18 is formed in 95% yield. This was reduced with L-Selectride to give 19 as a 14:1 mixture of diastereomers. Oxidation with ceric ammonium nitrate in THF gave the tricyclic dioxin 20 (75%) with the absolute configuration shown. As before, the relative configurations at the ring junctures were supported by NOE experiments, and these conform to a transition state orientation of the reacting components corresponding to structure 15b.

Work is in progress to elucidate the factors contributing to the high regioselectivity of nucleophile addition to 13b and to the high diastereoselectivity in the reactions of cyclohexanone enolate and related nucleophiles with this cationic complex. The reactions outlined above provide a new enantioselective route to dioxinofurans and their acyclic transformation products.

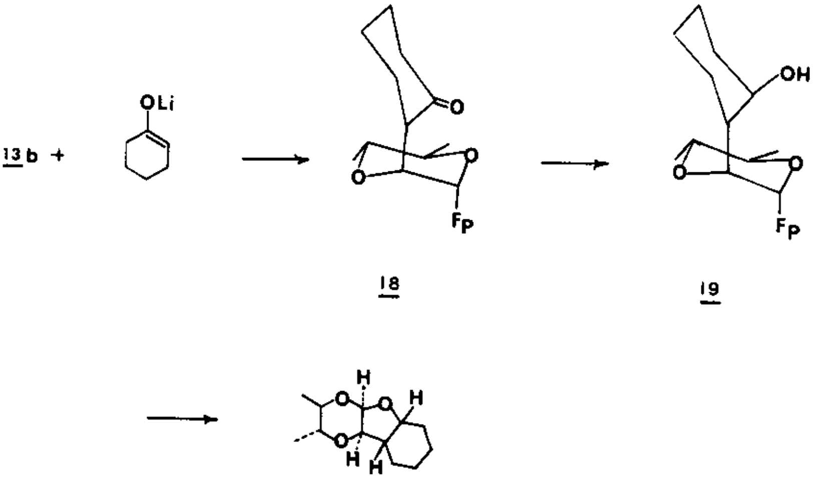


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TABLE I
Data for the X-ray Diffraction Study of $Cp(CO)_2Fe\text{-}(C_4H_6O_2)\text{-}C_6H_9O$ <u>14</u>

(A) Crystal Data at 21(1)°C.

Crystal system: monoclinic

Space group: $P2_1/c$ [C_{2h}^5; No.14]
$a = 12.857(3)$ Å
$b = 7.708(1)$ Å
$c = 17.960(4)$ Å
$\beta = 108.47(2)°$
$V = 1688.19$ Å^3

$Z = 4$

Crystal Size: 0.40 x 0.20 x 0.05 mm.
Formula Wt : 286.0
$\rho_{obs} = 1.380^a$ g-cm^{-3}
$\rho_{calc} = 1.417$ g-cm^{-3}
$\mu = 9.1$ cm^{-1} (Mo$K\bar{\alpha}$)

Cell constant determination : 12 pairs of ± (hkl) and refined 2θ, ω, X values in the range $23 \leq |2\theta| \leq 26°$ (λ(Mo$K\bar{\alpha}$) = 0.71073 Å)

(B) Measurement of Intensity Data

Radiation : Mo$K\bar{\alpha}$, graphite monochromator

Reflections measured: h, -k, ±l (to $2\theta = 50°$)

Scan type, speed : θ-2θ, vble, 1.95-3.91°/min

Scan range : symmetrical, $[0.9+\Delta(\alpha_2-\alpha_1)]°$

No. of reflections measured : 3394; 3239 in unique set

Standard reflections : 700, 4-4-3, 2-1-10; period 60
Absorption correction : empirical, normalized transmission factors 0.745-1.000

Data reduction: as before[b]

Statistical information : $R_{av} = 0.013$ (0kl reflections)

(C) Refinement

Refinement[d], with 2234 data for which $I > 1.96\sigma(I)$

Weighting of reflections : as before[c] , $p = 0.04$

Solution : Patterson, difference-Fourier

Refinement[d] : full-matrix least-squares, with anisotropic temperature factors for Fe, C and O atoms; isotropic temperature factors for H atoms (fixed at 0.95 Å C–H distance).
$R = 0.038$; $R_w = 0.043$; SDU = 1.41

Final difference map : 4 peaks, 0.278 e$^-$/Å^3 near C(9), 0.258 e$^-$/Å^3 near C(8) and 0.256 e$^-$/Å^3 an
0.245 e$^-$/Å^3 near Fe; other peaks random and ≤0.24 e$^-$/Å^3

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[a] Measured by neutral bouyancy in $C_2H_4Br_2$-CCl_4.

[b] B. M. Foxman, P. L. Goldberg and H. Mazurek, <u>Inorg.Chem.</u>, 1981, **20**, 4381; all computations in the present work were carried out using the ENRAF-NONIUS Structure Determination Package.

[c] P. W. R. Corfield, R. J. Doedens, and J. A. Ibers, <u>Inorg.Chem.</u>, 1967, **6**, 197.

[d] $R_{av} = \Sigma|I-I_{av}|/\Sigma I$; $R = \Sigma||F_o|-|F_c||/\Sigma|F_o|$; $R_w = \{\Sigma w[|F_o|-|F_c|]^2/\Sigma w|F_o|^2\}^{1/2}$
SDU = $\{\Sigma w[|F_o|-|F_c|]^2/(m-n)\}^{1/2}$ where m (=2234) is the number of observations and n (=280) is the number of parameters.

TABLE II[a]
Atomic Coordinates, Bond Distances (A) and Angles (Degrees)

Atom	x	y	z	Bond	Distance	Angle	Degrees
Fe	0.21456(3)	0.19284(5)	0.01832(2)	Fe-C(1)	1.733(3)	C(1)-Fe-C(2)	93.5(2)
O(1)	0.4500(2)	0.2237(4)	0.0596(2)	Fe-C(2)	1.751(3)	C(1)-Fe-C(8)	90.1(1)
O(2)	0.2278(2)	-0.1451(3)	0.0911(1)	Fe-C(3)	2.101(4)	C(2)-Fe-C(8)	85.6(1)
O(3)	0.1988(2)	0.0498(3)	-0.2190(1)	Fe-C(4)	2.100(4)	C(9)-O(3)-C(11)	111.1(2)
O(4)	0.1172(2)	-0.0533(3)	-0.0990(1)	Fe-C(5)	2.106(3)	C(8)-O(4)-C(10)	111.1(3)
O(5)	0.1750(2)	0.4562(3)	-0.2518(1)	Fe-C(6)	2.081(4)	Fe-C(1)-O(1)	178.4(3)
C(1)	0.3556(3)	0.2139(5)	0.0428(2)	Fe-C(7)	2.089(5)	Fe-C(2)-O(2)	179.6(3)
C(2)	0.2228(3)	-0.0117(4)	0.0623(2)	Fe-C(8)	2.058(3)	C(4)-C(3)-C(7)	106.8(3)
C(3)	0.1421(3)	0.3314(5)	0.0898(2)	O(1)-C(1)	1.156(4)	C(3)-C(4)-C(5)	110.1(4)
C(4)	0.0621(3)	0.2432(5)	0.0336(2)	O(2)-C(2)	1.144(4)	C(4)-C(5)-C(6)	108.3(3)
C(5)	0.0583(3)	0.2975(5)	-0.0386(2)	O(3)-C(9)	1.439(4)	C(5)-C(6)-C(7)	109.4(4)
C(6)	0.1356(3)	0.4210(5)	-0.0305(2)	O(3)-C(11)	1.425(4)	C(3)-C(7)-C(6)	105.5(3)
C(7)	0.1911(3)	0.4475(5)	0.0495(3)	O(4)-C(8)	1.434(4)	Fe-C(8)-O(4)	106.2(2)
C(8)	0.2107(2)	0.0592(4)	-0.0817(2)	O(4)-C(10)	1.426(4)	Fe-C(8)-C(9)	117.6(2)
C(9)	0.2024(2)	0.1649(4)	-0.1551(2)	O(5)-C(13)	1.200(4)	O(4)-C(8)-C(9)	108.1(2)
C(10)	0.1137(3)	-0.1677(4)	-0.1621(2)	C(3)-C(4)	1.371(5)	O(3)-C(9)-C(8)	109.7(2)
C(11)	0.1078(3)	-0.0656(5)	-0.2347(2)	C(3)-C(7)	1.418(7)	O(3)-C(9)-C(12)	106.0(3)
C(12)	0.2975(2)	0.2895(4)	-0.1481(2)	C(4)-C(5)	1.349(5)	C(8)-C(9)-C(12)	115.4(3)
C(13)	0.2665(3)	0.4340(4)	-0.2085(2)	C(5)-C(6)	1.351(5)	O(4)-C(10)-C(11)	110.2(3)
C(14)	0.3580(3)	0.5569(5)	-0.2079(2)	C(6)-C(7)	1.402(6)	O(3)-C(11)-C(10)	110.0(2)
C(15)	0.4609(3)	0.4620(6)	-0.2079(2)	C(8)-C(9)	1.525(5)	C(9)-C(12)-C(13)	112.3(2)
C(16)	0.4954(3)	0.3294(6)	-0.1425(3)	C(9)-C(12)	1.528(4)	C(9)-C(12)-C(17)	113.5(3)
C(17)	0.4030(3)	0.1983(5)	-0.1489(2)	C(10)-C(11)	1.503(5)	C(13)-C(12)-C(17)	111.4(3)
				C(12)-C(13)	1.516(4)	O(5)-C(13)-C(12)	123.4(4)
				C(12)-C(17)	1.531(5)	O(5)-C(13)-C(14)	121.2(4)
				C(13)-C(14)	1.508(5)	C(12)-C(13)-C(14)	115.4(2)
				C(14)-C(15)	1.513(6)	C(13)-C(14)-C(15)	112.1(3)
				C(15)-C(16)	1.514(7)	C(14)-C(15)-C(16)	111.6(4)
				C(16)-C(17)	1.536(5)	C(15)-C(16)-C(17)	111.0(3)
						C(12)-C(17)-C(16)	111.3(4)

Estimated standard deviations in the least significant digit appear in parentheses.

[a] A figure showing complete thermal ellipsoid detail and tables of (a) structure factors and (b) thermal parameters are available from the authors.

EXPERIMENTAL

Reactions were carried out using standard Schlenk technique under an argon atmosphere. THF and Et_2O were distilled under nitrogen from sodium/benzophenone. Methylene chloride was distilled under nitrogen from CaH_2. IR spectra were recorded on a PE-683 spectrophotometer in methylene chloride solution and referenced to polystyrene. ^1H NMR spectra were recorded on a Varian EM-390 or Varian XL300 (NIH-1-S10RR01493-01-A1) and referenced to internal TMS. ^{13}C NMR spectr were recorded on a Varian XL300 spectrometer and referenced to solvent. Alumina refers to basi alumina activity four unless otherwise noted. Petroleum ether refers to the fraction boiling 20-40 °C. L-Selectride and n-butyl lithium were purchased from Aldrich Chemical and used without further purification. (R,R)-2,3-butanediol was purchased from Strem Chemical and used without further purification.

Threo-1-[dicarbonyl-η-cyclopentadienyliron(II)]-2-(2'-oxocyclohexyl)-1,2-diethoxyethane 4 - Lithium cyclohexanone enolate (1.5 mmol) was generated as in the synthesis of 14 below in 10 ml of THF and cooled to -78 °C. Fp-cis-1,2-diethoxyethene tetrafluoroborate 3b (0.532 g, 1.40 mmol) was added in one portion as the solid and stirred until no ppt was apparent (approx. 3 h). Ether (30 ml) was added and the mixture filtered through alumina, washing the alumina twice with 10 ml of ether. The solvent was removed in vacuo and the residue chromatographed on alumina with 20% ether/petroleum ether, collecting the mobile yellow fraction. The solvent was removed in vacuo to give a bright yellow oil, 0.447 g (82%). IR (CH_2Cl_2) 2007,1945 (C=O) 1707 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.40 (d,1H,J=3.0Hz,Fp-CH) 4.85 (s,5H,Cp) 3.8-3.1 (m,5H,Fp-$CH\underline{H}$, O-CH_2's) 2.9 (m,1H,$C\underline{H}$-C=O) 2.5-1.0 (b,8H,$C\underline{H}_2C\underline{H}_2C\underline{H}_2C\underline{H}_2$) 1.20 (t,3H,J=7.0Hz,$CH_3$) 1.10 (t,3H, J=8.0Hz,$CH_3$); ^{13}C NMR ($CDCl_3$) δ 218.2,216.3 (C=O) 213.0 (C=O) 86.0 (Cp) 88.2,80.2 (Fp-$\underline{C}H\underline{C}H$) 66.4,65.8 ($CH_2O$'s) 54.5 ($\underline{C}$HC=O) 42.4 ($\underline{C}H_2$C=O) 29.9,27.3,24.6 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 15.8,15.4 ($CH_3$). Anal. Calcd for $C_{19}H_{21}FeO_5$: C, 58.50; H, 6.72. Found: C, 59.11; H, 6.05.

1-[Dicarbonyl-η-cyclopentadienyliron(II)]-2-(2'-cis-hydroxycyclohexyl)-1,2-diethoxyethane 5 -

Compound 4 (0.370 g, 0.949 mmol) was dissolved in 10 ml of THF and cooled to -78 °C. L-Selectride (1.14 ml, 1 M, 1.14 mmol) was added via syringe and the mixture stirred for 2 h. Methanol (1 ml) was added and stirred for 1/2 h. Ether (20 ml) was added and the mixture filtered rapidly through alumina, washing the alumina with 2x20 ml of ether. The solvent was removed in vacuo and the residue extracted with 3x10 ml ether. The ether extracts were combined and the solvent removed in vacuo to give 0.521 g of a bright yellow oil. ^1H NMR shows the presence of tri-secbutylborane in the mixture. Attempts to purify the product by chromatography on either alumina or silica gel resulted in significant decomposition and product rearrangement (see text). It was found that the presence of the borane did not interfere with subsequent reactions. Estimated yield from ^1H NMR integration - 90%. IR (CH_2Cl_2) 2010,1945 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.95 (d,1H,J=9Hz,FpCH) 4.80 (s,5H,Cp) 4.1-3.3 (b,6H,OCH's OCH_2's) 1.0-2.0 (b,signals overlap with borane); ^{13}C NMR - δ 217.0,216.3 (C=O) 95.4,82.4,66.8 (O-$\underline{C}HC_2$) 69.2,67. (O-$\underline{C}H_2$) 41.5 ($C_3\underline{C}H$) 32.2 (HOCH$\underline{C}H_2$) 26.7,26.0,19.8 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 15.9,15.6 ($CH_3$).

Cis-3a,4,5,6,7,7a-hexahydrobenzofuran 7 -

Compound 4 (0.92 g, 2.36 mmol) was dissolved in 15 ml of THF and cooled to -78 °C. L-Selectride (2.36 ml, 1.0 M, 2.36 mmol) was added dropwise via syringe and stirred for 1 h. MeOH (0.5 ml) was added followed by 15 ml of ether and the mixture was filtered through a short plug of alumina, washing the alumina with 2x10 ml of ether. The solvent was removed to give 1.02 g of a red oil. Chromatography on alumina with 10% ether/petroleum ether led to decomposition of the Fp containing product as evidenced by retention of color on the column even after elution with 100% ether. Removal of solvent from the collected eluent gave a pale yellow oil, 0.176 g (60%), which was identified as compound 7 by IR and ^1H NMR.

Cis-anti-cis-perhydro-2,3-diethoxybenzofuran 9 -

Method A). The mixture of 5 and tri-sec-butylborane (est. max. of 5 - 0.371 g, 0.949 mmol) was dissolved in 10 ml of THF, cooled to 0 °C and saturated with CO at atmospheric pressure. Ceric ammonium nitrate (3.12 g, 5.69 mmol, 6 eq.) was added as a single portion and stirring continued for 1 h. Addition of 20 ml of water and 40 ml of Et_2O formed two layers. The organic layer was separated and the aqueous layer extracted with 3x20 ml of ether. The combined organic layers were dried over $MgSO_4$ and the solvent removed in vacuo to give a yellow oil. The oil was taken up in ether, filtered through alumina to remove traces of metal salts and the solvent removed in vacuo to give 0.112 g (55% from 4) of a pale yellow oil. IR (neat) 2920b,1635,1450,1375, 1110b,1010b cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.01 (d,1H,J=5.4Hz,O_2CH) 3.94 (m,2H,$OC\underline{H}C_2$'s) 3.81 (m,1H,one OCH_2) 3.65-3.45 (m,3H,three OCH_2) 2.15 (m,1H,$C\underline{H}[CH]_2$) 2.00-1.25 (m,8H,ring CH_2's) 1.25 (m,6H,CH_3's). ^{13}C NMR ($CDCl_3$) δ 100.7 ($O_2\underline{C}H$) 82.2,74.0 ($O\underline{C}HC_2$) 65.8,63.3 ($O-\underline{C}H_2$) 38.3 ($C_3\underline{C}H$) 28.9 ($O-CH-\underline{C}H_2$) 23.7,21.5,20.2 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 15.5,15.2 ($CH_3$). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.11; H, 10.14.

Method B) (One-pot synthesis). Lithium cyclohexanone enolate (1.78 mmol) was generated in 25 ml of THF as in the synthesis of 14 below and cooled to -78 °C. Compound 3b (0.61 g, 1.62 mmol) was added in a single portion and stirred for 2 h. L-Selectride (1.62 ml, 1 M, 1.62 mmol) was added and stirred an additional hour. Ceric ammonium nitrate (5.31 g, 9.72 mmol) was added, the mixture warmed to 0 °C and stirred 1 h (Note: CO atmosphere was not used for this reaction). Addition of 75 ml of ether precipitated the cerous nitrate and other salts. The mixture was filtered and the solvent removed in vacuo to give a red oil. The oil was chromatographed on alumina with petroleum ether followed by 5% ether/petroleum ether to give two compounds, 10 (0.029 g) and 9 (0.160 g, total 52% yield for three steps). The partial epimerization appears to have taken place during the chromatography as no sign of 10 was visible in the ^{1}HNMR of the crude product. A third fraction (0.025 g) of an unidentified material was also collected which shows a ^{1}HNMR spectrum similar to 9 and 10, but shows a complex pattern near 5.0 ppm, the shift of the acetal carbon.

Trans-anti-cis-perhydro-2,3-diethoxybenzofuran 10 -

The epimerization was carried out via a modification of the procedure of Rozinek et al.[17] Compound 9 (0.056 g, 0.26 mmol) was dissolved in 5 ml of absolute ethanol, dry HCl gas bubbled through the solution for 2 min and the mixture then refluxed for 1 h. The solution was cooled to room temperature and N_2 bubbled through the solution for 1 h to purge the HCl. The remaining solvent was removed in vacuo, the residue taken up in ether and filtered through alumina. The solvent was removed to give 0.041 g (74%) of a colorless oil. ^1H NMR ($CDCl_3$) δ 4.98 (d,1H, J=3.60Hz, O_2CH) 4.20 (m,1H,$O-C\underline{H}CH_2$) 3.89 (d of d,1H,J=3.60Hz,6.00Hz,$O_2CHC\underline{H}$) 3.79 (d of q, 1H,J_d=9.60Hz J_q=7.20Hz,one OCH_2) 3.51 (m,3H,three OCH_2) 2.15 (m,1H,$C\underline{H}[CH]_2$) 2.0-1.1 (b,8H,ring CH_2's) 1.23,1.20 (two t,6H,J=7.20Hz,CH_3's); ^{13}C NMR ($CDCl_3$) δ 106.7 (O_2CH) 87.7, 75.1 ($O\underline{C}HC_2$) 65.7,63.9 (OCH_2's) 40.5 ($C_3\underline{C}H$) 27.9 ($OCH\underline{C}H_2$) 23.9, 21.7,20.3 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 15.5,15.2 ($CH_3$'s).

Dicarbonyl-η-cyclopentadienyliron(II)-η-5,6-dihydrodioxin tetrafluoroborate 13a - Fp-*cis*-dimethoxyethene tetrafluoroborate 3a (2.00 g, 5.7 mmol) was slurried in 10 ml of CH_2Cl_2 at 0 °C and ethylene glycol (1.56 ml, 1.76 g, 28.5 mmol, 5 eq) added. After about 5 min the solution became homogeneous and then a ppt formed. The mixture was stirred for an additional 15 min then 10 ml of ether added and the mixture filtered, washing the ppt with 3x5 ml of ether. Drying under vacuum gave a bright yellow solid, 1.92 g (97%). IR (CH_3NO_2) 2070,2030 (C=O) cm^{-1}; ^1H NMR (CD_3NO_2) δ 7.75 (bs, 2H,CH=CH) 5.50 (s,5H,Cp) 4.05 (m,4H,CH_2CH_2); ^{13}C NMR (CD_3NO_2) δ 210.9 (C=O) 102.7 (CH=) 89.3 (Cp) 67.4 (CH_2). Anal. Calcd for $C_{11}H_{11}BF_4FeO_4$: C, 37.76; H, 3.17. Found: C, 37.76; H, 3.17.

Trans-2-[dicarbonyl-η-cyclopentadienyliron(II)]-3-(2'-oxocyclohexyl)-dioxane 14 - 1-Cyclohexenyltrimethylsilyl ether (0.255 g, 1.50 mmol) in 10 ml of THF was cooled to 0 °C and n-butyl lithium (0.685 ml, 2.2 M, 1.50 mmol) added dropwise via syringe over a five minute period. The mixture was stirred for one hour then cooled to -78 °C. Fp-dioxene-tetrafluoroborate 13a (0.50 g, 1.43 mmol) was added as a single portion and stirred until no ppt was visible (approx. 1.5 h). Ether (10 ml) was added and the mixture filtered through alumina and the alumina washed with 2x10 ml of ether. The organic layers were combined and the solvent removed in vacuo to give a yellow-brown solid (0.494 g, 96%). IR 2015,1955 (C=O) 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.05 (d,1H,J=7Hz,Fp-$C\underline{H}$) 4.85 (s,5H,Cp) 4.25 (d of d,1H,J=7Hz,3Hz, O-$C\underline{H}CH$-Fp) 3.7 (m,4H,O-$C\underline{H}_2C\underline{H}_2$-O) 2.8 (m,1H,$C\underline{H}C$=O) 2.4 (m,2H,$C\underline{H}_2C$=O) 1.9 (broad,6H,$C\underline{H}_2C\underline{H}_2C\underline{H}_2$). ^{13}C NMR ($CDCl_3$) δ 216.5 (C=O) 213.9 (C=O) 85.7 (Cp) 82.0,79.1 (O-CH-CH-O) 69.3,65.9 (O-CH_2CH_2-O) 52.1 ($\underline{C}HC$=O) 42.0 ($\underline{C}H_2C$=O) 26.3,26.0,24.0 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$). Anal. Calcd for $C_{17}H_{20}FeO_5$: C, 56.69; H, 5.60. Found: C, 56.72; H, 5.40.

Trans-2-[dicarbonyl-η-cyclopentadienyliron(II)]-3-(cis-2'-hydroxycyclohexyl)-dioxane 16 - Compound 14 (0.410 g, 1.13 mmol) was dissolved in 15 ml of THF and cooled to -78 °C. L-Selectride (1.13 ml, 1 M, 1 eq.) was added and the reaction stirred for 1 h at which time IR spectroscopy showed no sign of the organic carbonyl. Methanol (1 ml) was added and the mixture stirred for an additional 1 h. Ether (10 ml) was added, the mixture filtered through alumina and the alumina washed with 2x10 ml of ether. The solvent was removed in vacuo to give a red-brown solid. Trituration with 5 ml of petroleum ether at 0 °C gave a yellow crystalline solid (0.36 g, 87%). IR (CH_2Cl_2) 2020,1960 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.85 (s,5H,Cp) 4.80 (d,1H,Fp-CH) 4.2-3.6 (m,6H,O-$C\underline{H}_2C\underline{H}_2$-O $OC\underline{H}$'s) 2.0-1.2 (b,9H,$C\underline{H}[C\underline{H}_2]_4$); ^{13}C NMR δ 216.2,215.9 (C=O) 91.4

(CHOH) 85.6 (Cp) 79.1,72.3 (Fp-$\underline{C}$H-$\underline{C}$H) 71.2,67.6 (O-$\underline{C}H_2\underline{C}H_2$-O) 43.0 (CHOH-$\underline{C}$H) 33.4 (CHOH-$\underline{C}H_2$) 25.3,19.7(2) ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$). Anal. Calcd for $C_{17}H_{22}FeO_5$: C, 56.38; H, 6.12. Found: C, 56.31; H, 6.29.

Cis-anti-cis-perhydro-1,4-dioxino[2,3b]benzofuran 17 -

Compound 16 (0.343 g, 0.95 mmol) was dissolved in 15 ml of THF saturated with CO, cooled to 0 °C and ceric ammonium nitrate added (3.12 g, 5.7 mmol, 6 eq.). Work-up followed the procedure outlined in the synthesis of 9 above. Kugelrohr distillation gave a white crystalline solid (0.11 g, 63%). IR (neat) 2930,1140,1105,1052,995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.37 (d,1H,J=2.56Hz,O_2CH) 4.65 (m,1H,OC$\underline{H}$CH$_2$) 4.01 (d of d of d,1H,J=3.9Hz 10.1Hz 11.7Hz,one OCH_2) 3.68 (m,3H,$O_2CHC\underline{H}$ two OCH_2's) 3.52 (app d of t,1H,J_d=11.7Hz J_t=1.8Hz,one OCH_2) 2.06 (m,2H,$C\underline{H}C_3$ and one other) *1.70-0.90 (b,7H,remaining* CH_2*'s);* ^{13}C *NMR* ($CDCl_3$) δ *98.1* (CHO_2) *77.2,77.1 (O*$\underline{C}$*H) 63.8,59.9* (O-$\underline{C}H_2\underline{C}H_2$-O) 43.8 ($C_3\underline{C}H$) 28.4,24.2,23.7,19.8 (-$\underline{C}H_2\underline{C}H_2\underline{C}H_2\underline{C}H_2$-). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.92; H, 8.94.

Dicarbonyl-η-cyclopentadienyliron(II)-η-(R,R)-trans-5,6-dimethyl-5,6-dihydrodioxintetrafluoroborate 13b -

Fp-cis-dimethoxyethene tetrafluoroborate 3a (1.87 g, 5.3 mmol) was slurried in 15 ml of CH_2Cl_2 at 0 °C and (R,R)-2,3-butanediol (0.97 ml, 0.95 g, 10.6 mmol) added. After stirring for 1 h the solvent was removed in vacuo. CH_2Cl_2 (15 ml) was then added, the mixture stirred for an additional 0.5 h and the solvent removed in vacuo again. A third 15 ml portion of CH_2Cl_2 was added and stirred for 0.5 h followed by addition of 30 ml of ether. The resulting ppt was filtered, washed with 10 ml of 30% CH_2Cl_2/ether and then 10 ml of ether. Drying under vacuum gave an orange powder, 1.78 g (89%). IR (CH_2Cl_2) 2060,2025 (C=O) cm^{-1}. ^1H NMR (CD_3NO_2) δ 7.70 (d,1H,J=1.5Hz,CH=) 7.25 (d,1H,J=1.5Hz,=CH) 5.50 (s,5H,Cp) 3.60 (m,1H,O-CH) 3.45 (m,1H,O-CH) 1.30 (d,3H,J=4.5Hz,CH_3) 1.20 (d,3H, J=4.5Hz,CH_3). ^{13}C NMR (CD_3NO_2) δ 211.2,210.5 (C=O) 108.6,95.5 (CH=CH) 89.1 (Cp) 76.4,75.4 (O-CHCH-O) 16.7 (broad,CH_3). Anal. Calcd for $C_{13}H_{15}BF_4FeO_4$: C, 41.32; H, 4.00. Found: C, 40.40; H, 3.67.

Trans-2-[dicarbonyl-η-cyclopentadienyliron(II)]-3-(2′-oxocyclohexyl)-trans-5,6-(R,R)-dimethyldioxane 18 -

Lithium cyclohexanone enolate (2.78 mmol, 5% excess) was generated in 10 ml of THF as in the synthesis of 14 above and cooled to -78 °C. Compound 17 (1.00 g, 2.65 mmol) was added as a single portion and stirred until no ppt was visible (2 h). The mixture was diluted with 10 ml of ether and filtered through alumina, washing the alumina with 2x10 ml of additional ether. The solvent was removed in vacuo to give a viscous yellow oil. Chromatography on alumina with 50% ether/pet ether removed traces of unreacted silyl enol ether and gave a viscous yellow oil (0.95 g, 95%). CH analysis attempts were consistantly high in carbon, presumably due to trapped solvent. Successful analysis of derivitive 19 was obtained. IR (CH_2Cl_2) 2015,1948 (C=O) 1708 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.15 (s,1H, Fp-CH) 4.90 (s,5H,Cp) 3.60 (d,1H,J=10Hz,Fp-$CHC\underline{H}$) 3.25 (m,2H, Me-$C\underline{H}C\underline{H}$-Me) 1.9 (broad,9H,cyclohexyl) 1.10,1.05 (two d,6H,J=6Hz, $\underline{Me}$-CHCH-$\underline{Me}$); ^{13}C NMR ($CDCl_3$) 217.7,217.0 (C=O) 213.4 (C=O) 85.8 (Cp) 80.7,77.0 (Fp-$\underline{C}H\underline{C}H$) 71.0,69.5 (Me-$\underline{C}H\underline{C}H$-Me) 51.1 ($\underline{C}HC{=}O$) 42.8 ($\underline{C}H_2C{=}O$) 30.7,27.3,24.8 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 17.4,17.0 (Me's).

Trans-2-[dicarbonyl-η-cyclopentadienyliron(II)]-3-(cis-2'-hydroxycyclohexyl)-trans-5,6-(R,R)dimethyldioxane 19 -

Compound 18 (0.937 g, 2.42 mmol) was dissolved in 10 ml of THF, cooled to -78 °C, L-Selectride (2.42 ml, 1 M, 2.42 mmol) added. After 1 h, 1 ml of methanol was added and stirred for 20 min followed by 10 ml of ether. The mixture was filtered through alumina, washing the alumina with 2x10 ml of ether, and the solvent removed in vacuo to give a yellow oil. Chromatography on alumina with 20% ether/pet ether gave two fractions, unreacted 18 (0.312 g, 33%) and 19 (0.47 g, 75% corrected for recovered 18) as a yellow shellac. IR (CH_2Cl_2) 2010,1948 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.55 (s,1H,Fp-CH) 4.85 (s,5H,Cp) 4.05 (b,1H,$C\underline{H}OH$) 3.40 (m,4H,$O\underline{H}$ $CH_3C\underline{H}$ $FpCHC\underline{H}$) 2.10-0.95 (b,15H,$C\underline{H}_2$'s,$C\underline{H}_3$'s); ^{13}C NMR ($CDCl_3$) δ 86.4 (Cp) 83.7,74.0,71.6,69.5,67.7 ($O\underline{C}H$) 41.0 ($HOCH\underline{C}H$) 33.8 ($HOCH\underline{C}H_2$) 25.7,22.3,19.7 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 17.7,17.5 ($CH_3$). Anal. Calcd for $C_{19}H_{21}FeO_5$: C, 59.24; H, 5.50. Found: C, 58.96; H, 5.72.

(2R,3R,4aR,9aS,9bR)-Trans-2,3-dimethyl-cis-anti-cis-perhydro-1,4-dioxino[2,3b]benzofuran 20 -

Compound 19 (0.75 g, 1.95 mmol) and ceric ammonium nitrate (6.4 g, 11.6 mM, 6 eq) were combined in 15 ml of THF as in the synthesis of 9 above. Work-up and Kuglerohr distillation gave 0.30 g (73%) of a colorless oil. Estimated diastereomer ratio was 14:1 by both GC and 13CNMR. $[\alpha]_D^{20}$ = +57.04 ($CHCl_3$, 0.087); IR (neat) 2930,1139,1109,1060,1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.13 (d,1H,J=3.7Hz,O_2CH) 4.39 (app q,1H,J_{ave}=3.76,$OC\underline{H}CH_2$) 4.00 (d of d,1H,J=3.7Hz 8.0Hz, $O_2CHC\underline{H}$) 3.55 (d of q,1H,J_d=8.5Hz J_q=6.3Hz,$CH_3C\underline{H}$) 3.31 (d of q,1H,J_d=8.5Hz J_q=6.3Hz,$CH_3C\underline{H}$) 2.58 (app quintet, 1H,J_{ave}=6.6Hz, $C\underline{H}[CHO]_2$) 1.90-0.90 (m,8H,CH_2) 1.17 (d,3H,J=6.3Hz,CH_3) 1.10 (d,3H,J=6.3Hz,CH_3); ^{13}C NMR ($CDCl_3$) δ 96.9 ($O_2\underline{C}H$) 76.7, 75.1,72.5,70.0 ($O\underline{C}H$) 35.4 ($C_3\underline{C}H$) 29.7 ($OCH\underline{C}H_2$) 23.3,21.3,21.2 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2$) 17.6,16.6 ($CH_3$). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.47; H, 9.21.

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