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The η^4-Dienyl Tricarbonyliron Moiety in Heterocyclic Synthesis. A Rare 1,2-Migration of the Complexation Site as a Key Step for a Novel Stereoselective Preparation of *trans*-2,3-Disubstituted 1,4-Dioxanes

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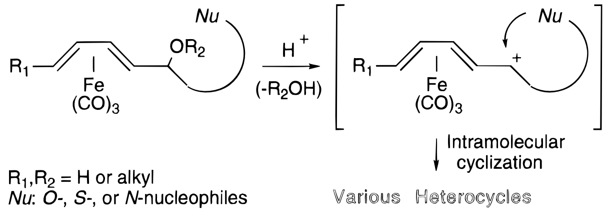
Synthetic studies performed in the context of an industrial project prompted us to consider existing routes to unusual heterocycles containing a 2,3-disubstituted 1,4-dioxane core. Surprisingly, sparse literature data made it obvious that currently known methods for the preparation of this type of heterocycles appeared not to be amenable to our needs, especially in their asymmetric versions. Specifically, no general preparation exists apart from isolated reports including (1) base-mediated intramolecular cyclization of the appropriate bromo alcohols;[1] (2) intramolecular electroreductive coupling of bis-activated olefins;[2] (3) sequential addition of nucleophilic free radicals derived from 1,4-dioxane to hexafluoropropene;[3] and (4) photochemical deoxygenation of a 5,6-disubstituted dioxanone.[4]

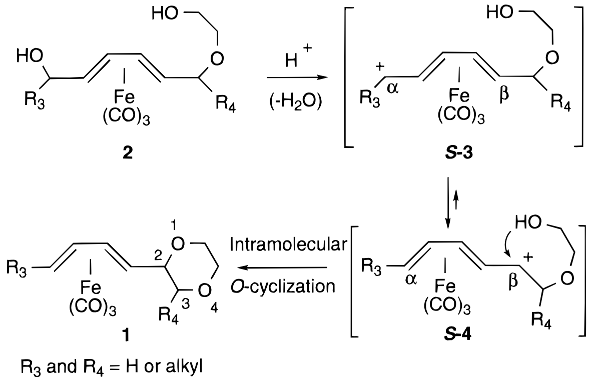
Having been strongly involved in the field of (η^4-dienyl)tricarbonyliron complexes for the last decade, we were aware of the well-known protecting and/or stereodirecting properties attached to the complexing $Fe(CO)_3$ unit just as well as the strong stabilization of carbocations located at the α position of the coordination site.[5−7] For example, by relying on the known electrophilicity of such (η^5-dienyl)tricarbonyliron(1+) cations and on the nature of a tethered pendant nucleophile *Nu*, their intramolecular trapping provides a useful route to various iron complexed chiral non racemic heterocycles,[8−13] as depicted in Scheme 1.

On the basis of related considerations, we designed the novel sequence outlined in Scheme 2 which would offer a direct entry to our required iron-complexed 2,3-disubstituted 1,4-dioxane **1**.

Scheme 1



Scheme 2



Worthy of mention are the three following sequential steps: formation of the transoid cation (*S*)-**3** generated *in situ*[14−16] by acidic dehydration (electronic deficiency at Cα) and isomerization of the complexation site by 1,2-migration of the $Fe(CO)_3$ unit,[17] thus revealing the second electrophilic center at Cβ in (*S*)-**4** followed by the expected *O*-cyclization. As a logical consequence of the equilibrium (*S*)-**3** ⇄ (*S*)-**4**,[5−7] consumption of (*S*)-**4** when forming **1** would favor the occurrence of this particularly unusual 1,2-shift of the $Fe(CO)_3$ unit. The potential of this sequence in heterocyclic synthesis proved quite attractive as demonstrated by the ready access to 2-substituted or 2,3-disubstituted 1,4-dioxanes **12** and **13**−**15** provided that (*S*)-**3** does not decompose before the shift nor react with other nucleophiles present in the medium (Scheme 3).

In order to test this proposed mode of *O*-heterocyclization, a screening of possible acidic reagents was carried out starting with the iron-complexed ether diol **8** as a model compound. Compound **8** was prepared in a straightforward manner from the known ester aldehyde **5**[18] (Scheme 3, three steps, 52% overall yield from **5**). Various acidic reagents among which *p*-toluenesulfonic acid, CF_3COOH, aqueous HBF_4, aqueous HBF_4/4Å molecular sieves, $HBF_4{\cdot}Et_2O$, aqueous H_2SO_4, and Amberlyst resin (acid form) under diverse conditions were rapidly screened with mixed success except the last reagent. This acidic resin promotes the expected *O*-cyclization of **8** (CH_2Cl_2, 20 °C) occurring with 1,2-

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(17) A migration of the $Fe(CO)_3$ moiety has been observed very recently during the bimolecular reaction of (η^4-dienyl)tricarbonyliron complexed *O*-acyl/phosphorylcyanohydrins with various heteronucleophiles; see: Takemoto, Y.; Yoshikawa, N.; Iwata, C. *J. Chem. Soc., Chem. Commun.* **1995**, 631−632.

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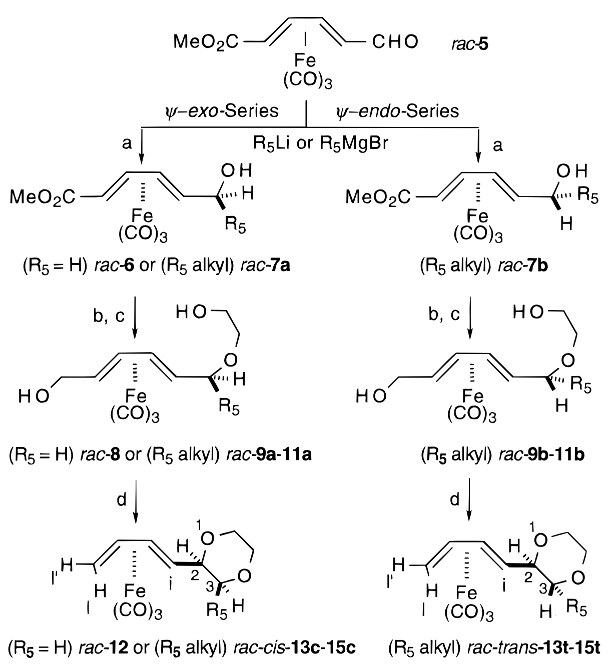
Scheme 3[a]



[a] (a) $NaBH_4$, MeOH, 20 °C, 1 hr, (R_5 = H, *rac*-**5** → *rac*-**6,** 96 %) or (R_5Li or R_5MgBr), THF, -78 °C, 1 hr, 77-97 % (*ψ-exo/ψ-endo* ~ 3/1); (b) N_2CHCO_2Et, cat. $[Rh_2(OAc)_4]$, CH_2Cl_2, 20 °C, 1 h, 46-80 %; (c) DIBAL-H, CH_2Cl_2, -78 °C, 1 hr, 63-82 %; (d) Amberlyst™ resin (acid form), CH_2Cl_2, 20 °C, 3-12 hrs

R_5	H	$n\text{C}_{16}\text{H}_{33}$		CH_2Cl		CH_2OBn	
rac-Substrate	**8**	**9a**	**9b**	**10a**	**10b**	**11a**	**11b**
rac-Product	**12**	**13c**	**13t**	**14c**	**14t**	**15c**	**15t**
yield (%)	65	10	50	38	91	20	72

migration of the $Fe(CO)_3$ unit. It results in the sole isolation of the monosubstituted (*E*)-iron-complexed dioxane **12** (65% isolated yield). This reagent minimizes decomplexed products (20% of the collected mass after purification), dimers of uncharacterized ether type (5–10%), and recovery of unreacted **8** (5–10%). Evidence for the *E* geometry of the complexed diene and its monosubstitution resulting from the 1,2-shift are supported by ^{1}H-/^{13}C-NMR data (supporting information).[16] Additionally, the highly shielded resonances of H_l (δ = 0.36 ppm) and of C_l (δ = 40.0 ppm) are consistent with the proposed structure.[16] Moreover, the *ψ-exo* relationship between the newly formed C2–O1 bond and the $Fe(CO)_3$ group (*anti* intramolecular addition) is secured by X-ray crystallographic analysis obtained for the two related *cis*- and *trans*-dioxanes **15c** and **15t** obtained at a later stage in this study.

We examined further the scope and limitations of this new *O*-heterocyclization by considering the diastereoisomerically pure *ψ-exo-/ψ-endo*-precursors **9**–**11**. These precursors were prepared in the same way as for **8** except that the *ψ-exo-/ψ-endo*-adducts **7a**/**7b** resulting from the addition of various organometallics on **5** were separated chromatographically and processed further.

Interesting aspects of these cyclizations can be highlighted. The *ψ-exo*-precursors **9a**–**11a** afford the *cis*-iron-complexed dioxanes **13c**–**15c** in rather low yields (10–38%) accompanied by numerous uncharacterized products in variable amounts, while *ψ-endo*-**9b**–**11b** lead to the corresponding *trans*-dioxanes **13t**–**15t** in moderate to good yield (50–91%). Similar ^{1}H-/^{13}C-NMR spectral trends support the depicted structures of the cyclized adducts (supporting information).[16] Especially indicative of the *cis-/trans*-nature of these complexed dioxanes are the two respective coupling constant values $J_{\mathrm{H2-H3}}$ = 3.0–3.1 and 8.2–8.6 Hz.[19] The X-ray structure of suitably grown monocrystals of **15c** and **15t** provide definitive structural confirmation and particularly established the *ψ-exo*-diastereoisomeric relationship between the newly formed C2–O1 bond and the $Fe(CO)_3$ unit. Although unclear in terms of mechanism, the observed stereoselectivity of the cyclization must be noticed and requires further studies for its understanding.

In conclusion, the present intramolecular and stereoselective *O*-heterocyclization involving (η^5-dienyl)tricarbonyliron(1+) *S*-shaped cations generated *in situ* provides a useful access to chiral-functionalized *trans*-2,3-disubstituted 1,4-dioxanes. As a new synthetic tool, the original key 1,2-shift of the $Fe(CO)_3$ unit expands the utility of such (η^4-dienyl)$Fe(CO)_3$ complexes. Its asymmetric version using the easily accessible chiral nonracemic **5**[18] and the chemical processing of these novel dioxanes are underway and will be reported in due course.

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Supporting Information Available: A detailed experimental procedure for the preparation of **12**–**15c/t** and spectroscopic characterization (6 pages).

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