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Glycosylmanganese pentacarbonyl complexes: an organomanganese-based approach to the synthesis of *C*-glycosyl derivatives

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This paper is dedicated to Professor Fausto Calderazzo.

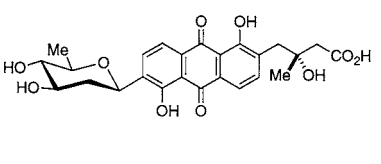
Abstract

Preparation, structure and reactions of glycosylmanganese pentacarbonyl complexes are discussed. Anomerically pure complexes of pyranosyl and furanosyl complexes were prepared in excellent yield. The conformations of the anomeric glucosyl and mannosyl complexes were derived from detailed analysis of their 1D and 2D ^{1}H- and ^{13}C-NMR spectra including NOE data. The complexes are further characterized by ^{55}Mn-NMR chemical shifts and ^{55}Mn, ^{13}C one-bond coupling constants. These compounds undergo various migratory insertion reactions resulting in formation of *C*-glycosyl derivatives. Applications of this technology to the synthesis of *C*-glycosyl and *C*-aryl glycosidic systems are discussed.

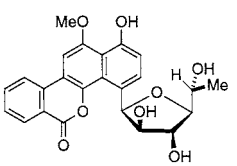
Keywords: *C*-glycoside; Conformation; Demetalation; Glycosylmanganese; Manganese pentacarbonyl; ^{55}Mn-NMR

1. Introduction

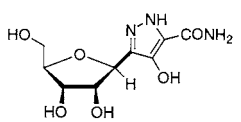
C-Glycosyl compounds are an interesting class of compounds due to their ability to function as nucleoside surrogates. As such, both naturally occurring and synthetic *C*-glycosyl derivatives have served as biochemical probes [1,2] and were shown to function as antibiotics [3–6], antitumor and antiviral agents [7]. For example, the naturally occurring *C*-glycosyls vineomycinone B_2 (**1**) [8–12], gilvocarcin M (**2**) [13], and pyrazofurin (**3**) [14–17] possess potent biological activity. Similarly, tiazofurin (**4**) and its synthetic analogue selenazofurin (**5**) are in clinical trials as antitumor agents [18,19].



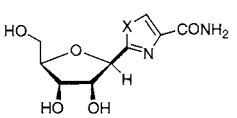
Vineomycinone B_2 (**1**)



Gilvocarcin M (**2**)



Pyrazofurin (**3**)



X = S, Tiazofurin (**4**)
X = Se, Selenazofurin (**5**)

The goal of this project was to develop a general approach to the synthesis of *C*-glycosyl derivatives based upon an extension of our previous studies into the chemistry of alkylmanganese pentacarbonyl com-

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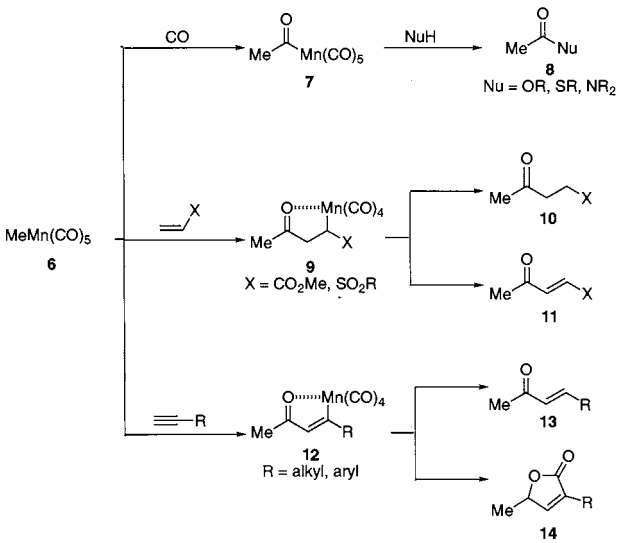


Scheme 1.

plexes [20–28]. As summarized in Scheme 1, it was demonstrated that simple alkyl complexes such as methylmanganese pentacarbonyl (**6**) can be transformed into a variety of carbonyl derivatives with formation of either one, two or three carbon–carbon bonds [22,23,25].

In the most common reaction of alkylmanganese complexes, ester, amide, and thioester derivatives (**8**) are prepared in excellent overall yield by the Reppe reaction. Migratory insertion of carbon monoxide affords the acyl complex **7** *with formation of a new carbon–carbon bond*. Cleavage of the acyl–metal bond by alcohols, amines, or thiols in the presence of Na_2CO_3 furnishes the respective carboxylic acid derivatives. This transformation, although well studied in the organometallic literature, will furnish new insights into the migratory insertion process when applied to complex glycosyl systems (vide infra).

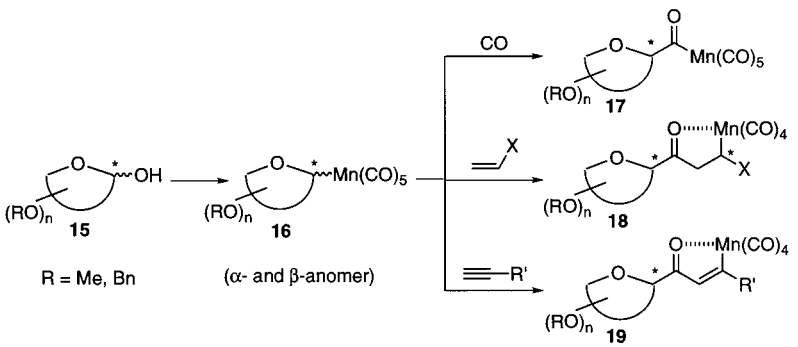
Sequential insertion of carbon monoxide and an electron-deficient alkene provides manganacycle **9**. Demetallation of complex **9** can be achieved either in a 'reductive' manner to furnish ketone **10** or to yield enone **11** with regeneration of the alkene moiety. The overall transformation occurs with formation of two carbon–carbon bonds, incorporation of one molecule of CO, and regioselective functionalization of the alkene substrate.

Finally, sequential insertion of an alkyne with methylmanganese pentacarbonyl gives the unsaturated manganacycle **12**. Two modes of demetalation of **12** have also been developed for this complex. In the first, protonation of the manganacycle provides enone **13**. This reaction was studied mechanistically in our laboratory [29].

Alternatively, hydride reduction of manganacycle **12** results in the incorporation of a second molecule of carbon monoxide and formation of butenolide **14**. This unique transformation involves formation of three carbon–carbon bonds, two molecules of CO being incorporated, and difunctionalization of an alkyne in a completely regioselective manner.

Having established the versatility of alkylmanganese pentacarbonyls for the preparation of carbonyl derivatives, it was our intention to extend these transformations to glycosylmanganese complexes as a means for preparing *C*-glycosyl derivatives (Scheme 2). Successful extension of the manganese methodology would require the investigation of several new aspects of this chemistry. First, it had to be demonstrated that glycosyl derivatives (**16**) could be prepared. With the exception of glycosyl iron [30], cobalt [31], and chromium carben [32,33], derivatives, stable transition metal analogues of carbohydrates have not been reported prior to our studies.

There were also stereochemical features to be considered. Glycosyl complex **16** could exist as either the α- or β-anomer, and it was our intention to synthesize **16** from the protected sugar derivative **15** in a highly stereoselective manner. This is a particularly important point because migratory and sequential insertion processes to give **17**–**19**, respectively, occur *with retention of configuration* [34]. Accordingly, the configuration of glycosyl complex **16** will be transferred to the *C*-glycosyl derivatives which result from migratory insertion.

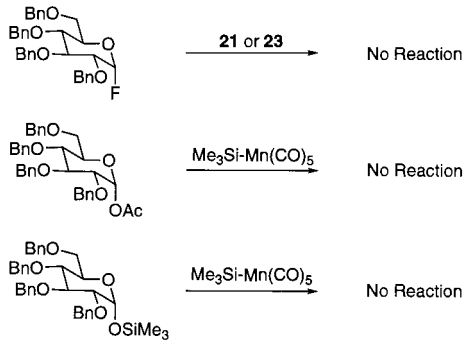


Scheme 2.

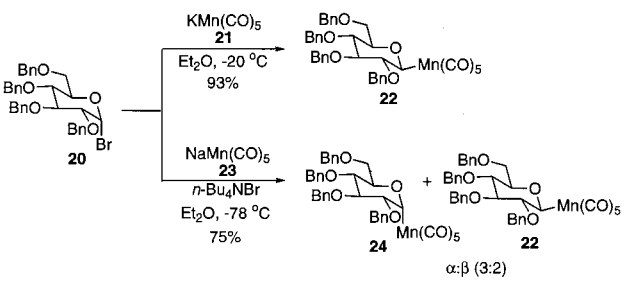
2. Preparation of pyranosyl- and furanosylmanganese pentacarbonyl complexes

Pyranosyl and furanosyl bromides and chlorides [35] react with alkali metal salts of the manganate anion to yield the corresponding glycosylmanganese pentacarbonyl complexes. In most instances, the condensation proceeds in excellent yield and is highly stereoselective. For example, α-glucopyranosyl bromide **20** and potassium manganate (**21**) react at −20°C to give β-complex **22** *exclusively* in virtually quantitative yield (Scheme 3) [36]. On the other hand, a mixture of α-complex **24** and β-complex **22** results from reaction of bromide **20** and sodium manganate (**23**) in the presence of tetrabutylammonium bromide at −78°C [21,36].

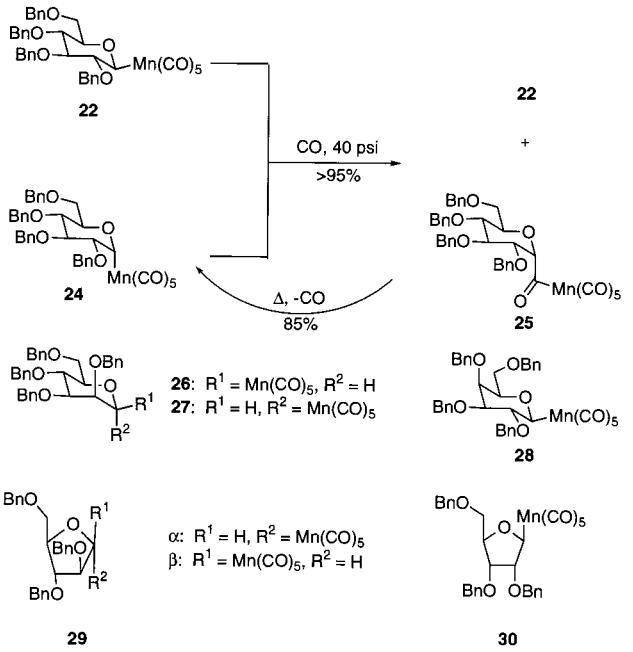
Condensation of sodium manganate **23** with bromide **20** is extremely sensitive to the purity of reagents and the ratios of anomeric products obtained (**22** vs. **24**) vary accordingly. Generally, α-anomer **24** predominates [21]. We attribute the change in stereoselectivity of the condensation in the presence of tetrabutylammonium bromide to in situ anomerization of the bromide. As the condensation proceeds, bromide ion is liberated and



reacts with **20** which results in formation of β-bromide. When the rate of condensation is rapid, as with potassium salt **21**, condensation proceeds more rapidly than anomerization and only β-complex is obtained. However, when the condensation rate is slower, as with **23**, anomerization occurs at a competitive rate to condensation, and mixtures of anomers are obtained. The α-anomer predominates under these conditions presumably because β-bromide is more reactive than α-bromide **20** [37,38]. Attempts to prepare the



Scheme 3.



Scheme 4.

glucopyranosyl complex(es) using the anomeric fluoride, acetate, or silyloxy derivatives, respectively, have not been successful [36].

Chromatographic separation of the α-and β-glucopyranosyl complexes **24** and **22**, respectively, cannot be accomplished. However, a chemical discrimination was developed. The α-complex **24** undergoes migratory insertion of carbon monoxide approximately seven times faster than β-complex **22** [39]. At 40 psi of carbon monoxide, it is possible to convert α-complex **24** to its acyl derivative **25** without inducing formation of the β-acyl complex (Scheme 4). Chromatographic separation of α-acyl **25** and β-glycosyl complex **22** is readily achieved. Gently warming the α-acyl complex induces deinsertion of CO and regenerates α-glucopyranosylmanganese pentacarbonyl (**24**).

Employing condensation conditions similar to those developed for the glucopyranosyl system, manganese pentacarbonyl complexes of the β- and α-mannopyranosyl (**26** and **27**), β-galactopyranosyl (**28**), α- and β-arabinofuranosyl (**29**) and β-ribofuranosyl (**30**) systems were synthesized [20,21,36,40].

Anomeric complexes of mannose derivatives **26** and **27** and arabinofuranosylmanganese pentacarbonyl (**29**) are separated in an analogous fashion to the glucopyranosyl analogs. In these instances, the relative rates of migratory insertion of α/β are $> 10^2$ and $> 10^3$, respectively [36]. This remarkable difference in the rates of migratory insertion in these systems is attributed to the orientation of the carbon–metal bond with regard to the lone pairs on oxygen (an anomeric effect?!) and may provide insight into the factors that control migratory insertion processes.

Table 1
^{1}H- and ^{13}C-NMR data (C_6D_6) of (glucosyl) $Mn(CO)_5$ complexes **22** and **24** and (β-pyranyl) $Mn(CO)_5$ (**31**)

Complex	δ (ppm)	^1J(C,H) (Hz)	H	δ (ppm)	^3J(H,H) (Hz)	
β-isomer (**22**)						
1	81.7	141	1	4.06	1,2	10.1
2	86.4	144	2	3.69	2,3	7.9
3	90.1	141	3	3.56	3,4	9.0
4	79.6	142	4	3.75	4,5	9.8
5	84.3	140	5	3.19	5,6a	4.1;2.0
6	69.8	142	6a,b	3.6–3.7	5,6b ^2J(6a,6b)	11.0
α-isomer (**24**)						
1	75.9	146	1	5.54	1,2	2.5
2	87.0	141	2	3.46	2,3	2.9
3	81.7	143	3	4.03	3,4	<3.5
4,5	76.9;76.4	144;144	4	4.09	4.5	7.5
			5	4.09	5,6a	3.2;2.3
6	70.5	141	6a,b	3.65–3.75	5,6b ^2J(6a,6b)	10.2
(*β-pyranyl*) *Mn(CO)*$_5$ (**31**)						
1	96.3	141	1	4.32	1a,2a	11.9
2	43.3	126;124	2e;2a	1.66;2.09	1a,2e	1.9
3	21.9	126;124	3e;3a	1.53;1.21	2a,3a	12.0
4	20.0	127;125	4e;4a	1.5;1.13	2a,3e	3.5
5	85.5	143;138	5e;5a	3.79;3.11	4a,5a	12.2
					4e,5a	2.1
					4e,5e	1.9
					^2J(2a,2e)	12.9
					^2J(5a,5e)	11.1

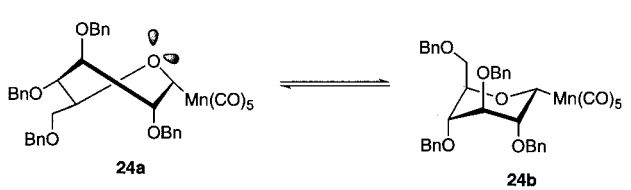
3. Structural characterization of glycosyl-Mn(CO)$_5$ complexes

3.1. ^{1}H- and ^{13}C-NMR spectra

^{1}H- and ^{13}C-NMR spectra provide unambiguous evidence for the configuration, anomeric purity and preferred conformation of the glycopyranosyl-$Mn(CO)_5$ complexes. The spectra were obtained with the perbenzylated glucosyl- and mannosyl-$Mn(CO)_5$ complexes and analyzed and assigned using homo- and heteronuclear 2D shift correlation experiments. For comparison, corresponding spectra were also obtained for pyranyl-$Mn(CO)_5$ (**31**) as a model complex. The results are collected in Table 1.

The β-glucosyl-isomer **22** shows the typical vicinal H,H-coupling pattern for a $^4C_1$ chair conformation with an equatorial $Mn(CO)_5$ group, i.e. large values of 8–10 Hz for ^3J(1,2), ^3J(2,3), ^3J(3,4), and ^3J(4,5). These diaxial coupling constants are 2–4 Hz smaller than in β-pyranyl complex **31**, presumably owing to the additional oxygen functions in the glucose fragments. No significant features are observable in the one-bond C,H coupling constants ($^1J(C,H) = 142 \pm 2$) Hz) of the >CH–O-groups, including the anomeric carbon.

The ^{1}H-NMR data of α-isomer **24** display an unusually deshielded resonance for the anomeric hydrogen H–C(1) (5.54 ppm) together with a slightly larger ^1J(C,H) value of 146 Hz. On the other hand, the H,H coupling data contain only small values (2.5–3.5 Hz) typical for a,e and e,e interactions, with the exception of $J(4,5) = 7.5$ Hz. These results are incompatible with $^4C_1$ conformation with an axial $Mn(CO)_5$ group and can be explained by a twist-boat conformation with a ψ-equatorial $Mn(CO)_5$ group displaying a large torsional angle (ca. 170°) for the H–C(4)–C(5)–H fragment. Only in this conformation H–C(1) is eclipsing the axial lone-pair on the ring oxygen that would explain the unusual deshielding of this proton by an electric field effect as well as the increased ^1J(C,H) coupling constant. [41] The twist-boat conformation **24a** is further confirmed by NOE experiments (vide infra) which, in addition, yield evidence for the $^1C_4$ chair conformation **24b** with an equatorial $Mn(CO)_5$ group, in equilibrium with the twist-boat **24a**.

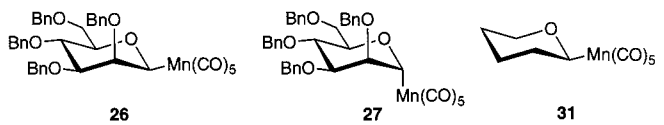


The corresponding ^{1}H- and ^{13}C-NMR data of the perbenzylated β- and α-mannosyl pentacarbonylmanganese complexes **26** and **27** are summarized in Table 2. As expected for the $^4C_1$ chair conformation **26** of the

Table 2
^{1}H- and ^{13}C-NMR data (C_6D_6) of (mannosyl) $Mn(CO)_5$ complexes **26** and **27**

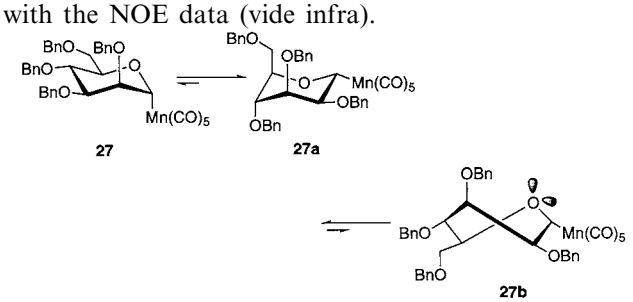
Complex	δ (ppm)	^1J(C,H) (Hz)	H	δ (ppm)	^3J(H,H) (Hz)	
β-isomer (**26**)						
1	81.4	140	1	4.31	1,2	<1
2	84.0	141	2	3.62	2,3	ca. 2.5
3	88.3	139	3	3.61	3,4	9.6
4	75.4	146	4	4.19	4,5	9.6
5	85.3	140	5	3.28	5,6a	4.7;1.4
6	70.3	142	6a,b	3.83	5,6b	11.3
				3.68	^2J(6a,6b)	
α-isomer (**27**)						
1	73.4	146	1	5.24	1,2	10.2
2	82.1	143	2	4.18	2,3	3.2
3	73.7	145	3	4.05	3,4	3.5
4	74.7	141	4	3.96	4,5	1.4
5	76.0	145	5	4.30	5,6a	7.5;6.5
6	68.8	142	6a,b	3.98	5,6b	9.3
				3.93	^2J(6a,6b)	

β-isomer the axial anomeric proton H–C(1) shows a normal resonance position at 4.31 ppm (**31**: 4.32 ppm) and only a very small vicinal coupling to the equatorial H–C(2) proton which is unresolved. Large values of 9.6 Hz are observed for ^3J(3,4) and ^3J(4,5). The rather large ^1J(C(4),H) coupling constant (146 Hz) may result from the influence of the 1,3-diaxial interaction with the lone-pair on the ring oxygen and the lone-pairs of the 3-hydroxy group (c.f. **24**).



26 **27** **31**

The proton spectrum of the α-isomer **27** shows a diaxial ^3J(1,2) coupling of 10.2 Hz that is incompatible with a $^4C_1$ chair conformation (axial $Mn(CO)_5$ group). The inverted $^1C_4$ chair (**27a**) or twist-boat (**27b**) with pseudo-equatorial $Mn(CO)_5$ and axial 3-hydroxy groups display torsional angles for the H–C(1)–C(2)–H fragment of ca. 180° and can be considered for the preferred conformation of the α-mannosyl complex. As shown by 2D-NOESY spectra, only (**27a**) is consistent with the NOE data (vide infra).



27 **27a**

27b

3.2. NOE studies

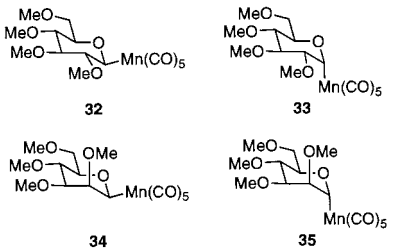
The results from proton and ^{13}C-NMR analysis as well as molecular mechanics calculation [42] are supported by NOE measurements. The α-mannosyl complex (**27b**) exhibits cross peaks in the 2D ^{1}H,^{1}H-NOESY spectrum for the following dipolar interactions: H–C(1)/Ha–C(6), Hb–C(6) (strong); H–C(2)/H–C(3) (strong); H–C(3)/H–C(4). There is, however, no detectable interaction within the diaxial pairs H–C(1)/H–C(4) or H–C(2)/H–C(5) as expected for a twist-boat conformation (**27b**). Thus the perbenzylated α-mannosyl pentacarbonylmanganese complex prefers the $^1C_4$ chair conformation (**27a**).

The situation is more complex for the α-glucosyl complex **24**. There is a strong dipolar interaction between H–C(1) and H–C(4) and a weaker one between H–C(1) and the C(6) methylene protons. The first NOE is clearly supporting the twist-boat conformation **24a** whereas the second one proves the presence of the inverted $^1C_4$ chair conformation **24b** in equillibrium with **24a**. A semiquantitative evaluation of conformer populations, however, is difficult since the cross peak intensities not only depend on H,H distances but also on magnetisation transfer effects, i.e. on the ratio of chair-to-boat interconversion rate and proton spin-lattice relaxation rate T_1^{-1} [43]. Nevertheless, as a consequence of the NOE results the observed vicinal H,H coupling constants have to be considered as average values for the respective dihedral arrangements in **24a** and **24b**. As an example, the largest observed value of 7.5 Hz for J(4,5) results from calculated dihedral angles of 177° in **24a** and 72° in **24b** (see Table 1) [42,44][1].

[1] Extensive molecular mechanics and dynamics optimizations of the carbohydrate complexes have been performed. All conformations 10 kcal mol^{-1} of the global minimum were optimized and evaluated for relative contributions to the equilibrium mixture.

3.3. ^{55}Mn-NMR spectra

We have made an attempt to prove potential differences in the C(1)–Mn bond in the four glycoside pentacarbonylmanganese complexes by ^{55}Mn-NMR. This quadrupolar nucleus gives rather broad lines for organomanganese complexes [27,45–47]. As it proved impossible to obtain ^{55}Mn-NMR signals for the perbenzylated derivatives, probably due to excessive line widths of >25 kHz because of long correlation times τ_c, the tetramethylethers (**32**–**35**) were prepared and measured in benzene-d_6 solution. The chemical shifts δ(Mn) and line widths $\Delta\nu(1/2)$ are presented in Table 3 together with the $^1J(^{55}Mn,^{13}C)$ coupling constants obtained by simulation of the ^{13}C line shapes as described earlier [45–47].



The ^{55}Mn chemical shifts lie in the narrow range of (-2058 ± 10) ppm, typical for alkylmanganese(I) pentacarbonyl complexes. The β-pyranyl reference complex (**31**) yields a chemical shift value of -2077 ppm. Taking into account the experimental error of ± 10 ppm in the determination of δ(Mn) for the rather broad resonances ($\Delta\nu(1/2) = 10$–14 kHz) a significant difference in shielding cannot be detected for the four complexes (**32**–**35**). Similarly, the one-bond C(1)–Mn(CO)$_5$ coupling constants lie in the narrow range of 46 ± 2 Hz characteristic for R–Mn(CO)$_5$ complexes [45]. The accuracy of these data is expected to be ± 2 Hz, and thus no significant differences are detected for the four glycosyl complexes. The $^1J(^{55}Mn,^{13}CO)$ values are also typical for manganese carbonyls and it is noteworthy that equatorial and axial carbonyls do not show the characteristic difference observed earlier for R–Mn(CO)$_5$ model complexes [45–47]. In this series of manganese complexes the one-bond coupling constants indicate that there is no significant difference in Mn–CO bond lengths for equatorial and axial CO groups [48] This observation was confirmed in the single-crystal X-ray analysis of β-glucosyl complex (**22**) in which the bond lengths of the axial and equatorial carbonyl groups were found to be virtually identical [49].

4. Migratory insertions of glycosylmanganese pentacarbonyl complexes

Having prepared glycosylmanganese pentacarbonyl complexes, we turned our attention to demonstrating that these complexes would undergo the processes indicated in Scheme 1. For the most part, the β-glucopyranosyl complex **22** was employed for these studies. When appropriate, an analogous reaction of the anomeric α-complex **24** was performed to demonstrate that migratory insertion reaction occurs with retention of configuration at the anomeric center [20,21,36,40].

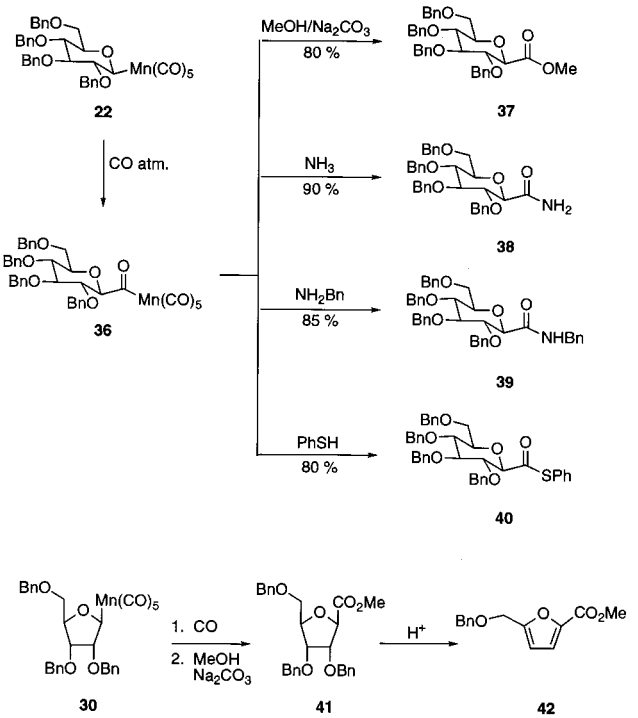
The Reppe reaction of β-glucopyranosyl complex **22** in the presence of alcohols, amines, or thiols occurs in excellent yield and complete stereoselectivity to afford the corresponding carboxylic acid derivatives (Scheme 5). In the case of β-ribofuranosyl complex **30**, formation of ester **41** constitutes a formal total synthesis of tiazofurin (**4**) and selenazofurin (**5**) [18,19]. Careful monitoring of conditions is mandated due to aromatization of ester **41** under carbonylation conditions.

C-Glycosyl ester **37** (also **38** and **39**) can be employed for the synthesis of a variety of heteroaromatic analogs as indicated in Scheme 6. Esters were transformed into isoxazole, imidazole, thiazole, and tetrazine derivatives employing established protocols [50]. Since both anomers of the glucopyranosyl system are available from the manganese methodology, it should be possible to prepare an array of *C*-glycosyl analogs for biological evaluation.

In the carbonylation of glycosylmanganese pentacarbonyls, a single carbon–carbon bond is formed. Sequential insertion, on the other hand, produces at least two new carbon–carbon bonds in the manganacycle products and it was gratifying to determine that in most instances the glycosyl complexes underwent sequential insertion efficiently. Scheme 7 summarizes a representa-

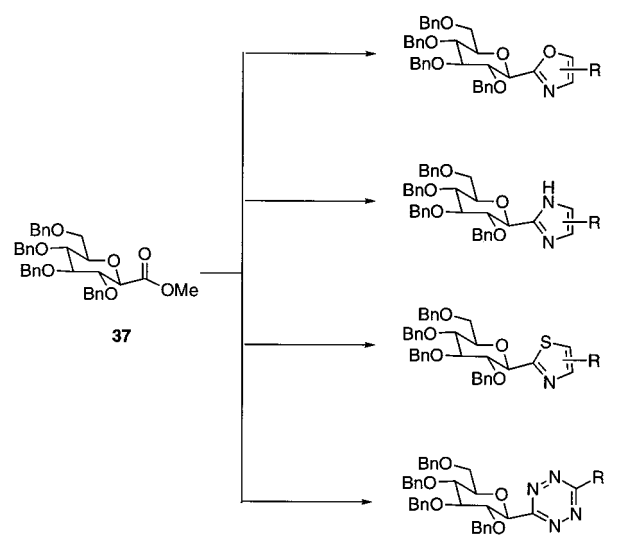
Table 3
^{55}Mn-NMR data of (glycosyl) Mn(CO)$_5$ complexes (C_6D_6, 300 K) and (β-pyranyl) Mn(CO)$_5$ ($CDCl_3$,300 K)

Complex	$\delta(^{55}Mn)$ (ppm)	$\Delta\nu(1/2)$ (kHz)	^1J(Mn,C(1)) (Hz)	$^1J(Mn,CO)_{eq}$	$^1J(Mn,CO)_{ax}$
β-Glucosyl (**32**)	−2059	12.06 ± 0.02	47	142	141
α-Glucosyl (**33**)	−2053	10.36 ± 0.03	48	147	–
β-Mannosyl (**34**)	−2056	13.77 ± 0.02	45	148	153
α-Mannosyl (**35**)	−2064	12.63 ± 0.03	46	135	139
β-Pyranyl (**31**)	−2077	13.20 ± 0.05	–	–	–



Scheme 5.

tive array of examples with β-glucopyranosyl complex **22.** As indicated, glucosylmanganese complex **22** undergoes sequential insertion with electron-deficient alkenes and terminal alkynes in analogy with the simple alkylmanganese complexes. Sequential insertion of methyl acrylate with **22** at 5 kba [51] yielded a 1:1 mixture of diastereomeric complexes **43**. We had hoped that the stereogenic center at the anomeric center would induce high diastereoselectivity in the sequential insertion process, but this was not observed with acrylate esters.



Scheme 6.

Similarly, sequential insertion of complex **22** with phenyl vinyl sulfone at 5 kbar provided a 1:1 mixture of diastereomeric manganacycles **44** (Scheme 7).

Insertion of methyl crotonate with complex **22** provided a 10:1 mixture of diastereomers **45**. Since the insertion of an alkene is known to occur in a *syn*-fashion, both diastereomers of manganacycles **45** should have the *anti*-relationship between methyl and carbomethoxy substituents. They differ only in the relative configurations relative to the anomeric center. The relative stereochemistry of the major diastereomer has not been determined. We propose that the excellent diastereoselectivity observed in insertion of crotonates is the result of the proximity of the stereogenic center to the anomeric center. In the transition state for migratory insertion, the stereogenic center at the anomeric carbon is close enough to the new stereogenic center to have an influence on the stereochemical course of the process. With acrylate esters, the new stereogenic center is too far from the existing anomeric center to be influenced. The excellent diastereoselectivity observed with crotonates suggests it may be possible to induce remote stereogenic centers in other sequential insertion processes.

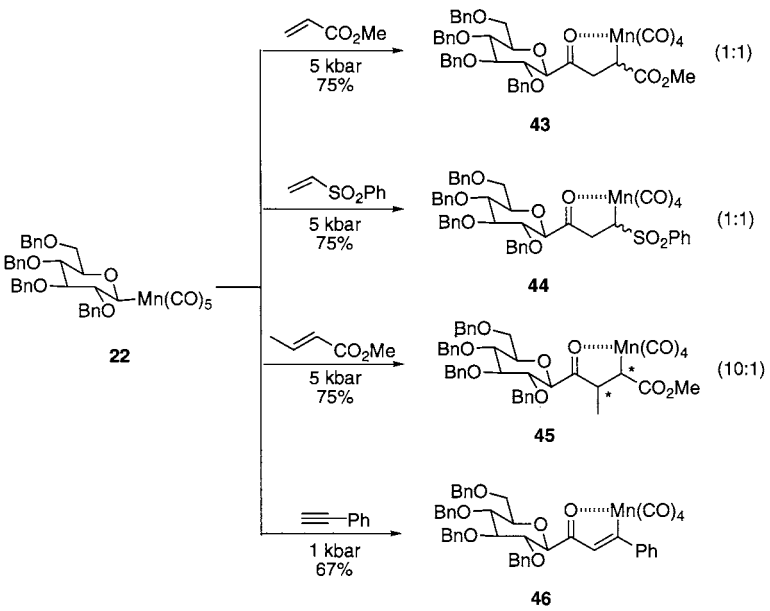
The sulfone adducts were not fully characterized due to their propensity to undergo elimination of phenylsufinic acid. However, the products of the elimination were stable and their characterization will be discussed below. [36]

Phenyl acetylene underwent regioselective insertion with complex **22** at atmospheric pressure to afford unsaturated manganacycle **46**. This result was analogous to the situation in simple alkylmanganese complexes where alkynes are more reactive toward sequential insertion and do not require high pressures to obtain good yields of manganacycles (Scheme 1) [22,25].

As anticipated, demetalation of manganacycle **43** could be accomplished photochemically in the presence of oxygen and water to produce enone **47** [29]. Alternatively, if the demetalation was performed in the absence of oxygen, then ketone **48** was the sole product of demetalation (Scheme 8). A discussion of the mechanism of this demetalation reaction has been published previously [25,52].

Treatment of ketone **48** with hydrazine (or its derivatives) gave dihydro-pyridazine **49** in good yield. Oxidation to pyridazine **50** has proven to be problematic in this instance. Enone **47**, on the other hand, reacts with hydrazine to afford dihydropyrazole **51** as a 1:1 mixture of diastereomers (Scheme 9) [36].

Manganacycle **44**, the product of insertion of phenyl vinyl sulfone with β-complex **22** (Scheme 10), was unstable and could not be fully characterized (vide supra). Photolysis of the crude manganacycle according to standard protocols provides keto-sulfone **52**. Sulfone **52**



Scheme 7.

is prone to loss of phenylsulfinic acid to give enone **53** [36].

When manganacycle **44** is allowed to remain in ether solution in the dark at atmospheric pressure, a single diastereomer of butenolide **55** (configuration unknown) is produced in excellent yield [36]. Presumably, the butenolide results from formation of manganacycle **54** by loss of phenyl sulfinic acid, protonation of **54**, migratory insertion of an additional molecule of CO producing ketene **57**, enolization, and ring formation. We have previously demonstrated that this mechanism is operative in reactions of acetylene derivatives [24].

5. Conclusion

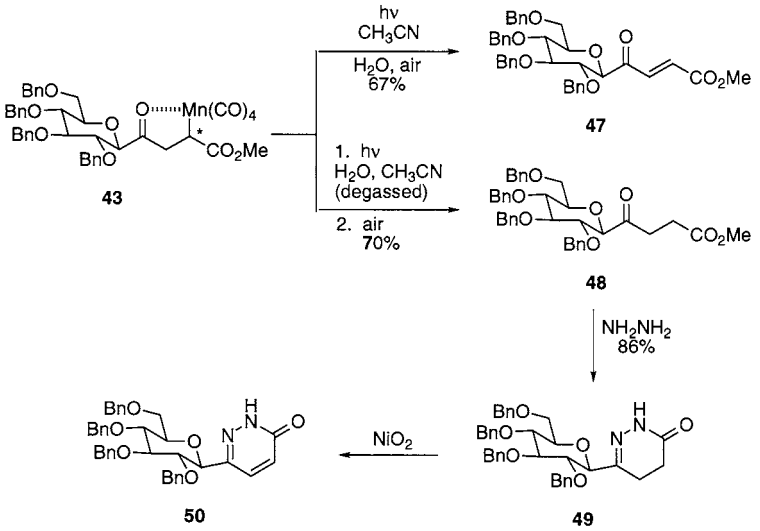
In this manuscript, the focus was on synthesis, characterization, and transformations of glycosylmanganese pentacarbonyl complexes. Highly stereoselective synthesis of pyranosyl and furanosyl complexes was accomplished by condensations of glycosyl bromides and chlorides. The conformations of the anomeric glucosyl and mannosyl complexes were derived from detailed analysis of their 1D and 2D proton and ^{13}C-NMR spectra including NOE data. The complexes are further characterized by ^{55}Mn-NMR chemical shifts and ^{55}Mn, ^{13}C one-bond coupling constants. The glycosyl complexes undergo a variety of migratory insertion processes resulting in formation of novel *C*-glycosyl derivatives.

6. Experimental

6.1. General

The ^{1}H-NMR spectra were measured at 200, 400 and 600 MHz, the ^{13}C spectra at 50.0, 100.6 and 150.9 MHz on a Bruker AF-200, AM-400 and AMX-600 spectrometers, respectively. 2D-COSY, TOCSY and NOESY experiments were performed using standard Bruker software. All chemical shifts are given relative to internal tetramethylsilane. ^{55}Mn-NMR spectra were recorded at 99.2 and 148.8 MHz on the same instruments and chemical shifts are referred to aqueous $KMnO_4$ as an external standard and ^{55}Mn, ^{13}C coupling constants were obtained by quantitative lineshape analysis of the ^{13}C resonances as described earlier [45–47]. Chemical shifts are reported in parts per million (δ) and coupling constants (J values) are given in Hertz (Hz). Infrared absorbances are reported in reciprocal centimeters (cm^{-1}).

Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium/benzophenone ketyl. Acetonitrile (MeCN), benzene and methylene chloride (CH_2Cl_2) were distilled from calcium hydride. Methanol (MeOH) and ethanol (EtOH) were dried and stored over molecular sieves. Glassware used in the reactions was dried overnight in an oven at 120°C. All reactions were performed under an atmosphere of argon unless noted otherwise. Dimanganese decacarbonyl ($Mn_2(CO)_{10}$) was obtained from Strem Chemical (Cata-



Scheme 8.

log no. 25-13330) and was sublimed (70°C/0.1 mmHg) prior to use.

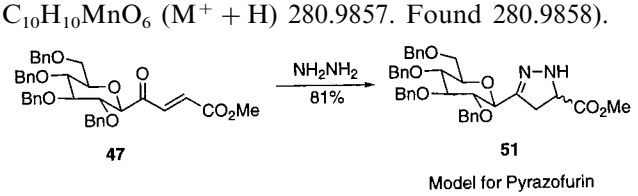
Preparation of compounds **24** [21], **26** [20], **27** [20], **28** [20], **29** [20], **30** [20], **32** [20], **41** [20], **43** [23] and **48** [23] were reported by the DeShong group.

6.2. 2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosylmanganese pentacarbonyl (22)

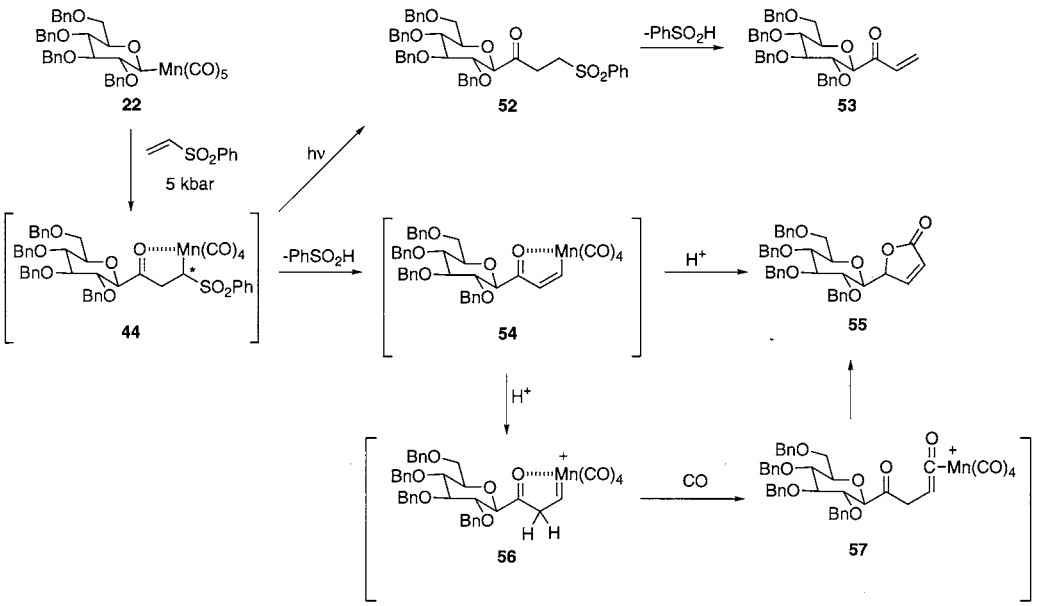
Glucopyranosylmanganese complex **22** was prepared from the corresponding α-bromide **20** [21]. Glucopyranosylmanganese complex **22** may also be prepared from the chloro-derivative of **20**. A solution of 3.24 g (5.8 mmol) of α-chloride [53,54], in 5 ml of anhydrous Et_2O was added via syringe to a freshly prepared solution of $KMn(CO)_5$ [54] in 10 ml of Et_2O at 0°C. The solution was stirred in the dark at 42°C for 12 h. The reaction was diluted with 10 ml of Et_2O and quenched with 0.1 ml of water until no hydrogen evolved. The mixture was dried over Na_2SO_4, filtered through Celite, and concentrated in vacuo. The red residue was purified by flash chromatography eluting with hexanes then 5% EtOAc/hexanes to give 3.9 g (93%) of β-anomer **22** as a yellow oil. The oil was crystallized from absolute methanol (avoiding excess heating and exposure to light) to give white needles. M.p. 69–70°C; $R_f = 0.66$ (33% EtOAc/hexanes). IR (CCl_4) 2013, 2050, 2013, 1988. ^{1}H-NMR (400 MHz, C_6D_6): δ 7.09–7.48 (m, 20 H) 5.28 (A of AB q, $J = 11.9$, 1H), 4.73 (B of AB q, $J = 11.9$, 1H), 5.00 (A of AB q, $J = 11.1$, 1H), 4.75 (B of AB q, $J = 11.1$, 1H), 4.80 (A of AB q, $J = 11.1$, 1H), 4.68 (B of AB q, $J = 11.1$, 1H), 4.64 (A of AB q, $J = 12.3$, 1H), 4.55 (B of AB q, $J = 12.3$, 1H), 4.06 (d, $J = 10.1$, 1H), 3.75 (dd, $J = 9.8$, 9.0, 1H), 3.70 (dd, $J = 11.0$, 4.1, 1H), 3.65 (dd, $J = 11.0$, 2.0, 1H), 3.69 (dd, $J = 10.1$, 7.9, 1H), 3.56 (dd, $J = 9.0$, 7.9, 1H), 3.19 (ddd, $J = 9.8$, 4.1, 2.0, 1H). ^{13}C-NMR (100 MHz, C_6D_6) δ 211.5, 209.6, 139.2, 139.0, 138.7, 128.5–127.5, 90.1, 86.4, 79.6, 78.4, 77.8, 75.5, 74.8, 73.6, 69.8. MS: m/z Calc. for $C_{34}H_{36}O_5$ $[(M^+ + H) - Mn(CO)_5]$ 524.2547. Found 524.2563.

6.3. 2-Manganese pentacarbonyl tetrahydropyran (31)

A solution of tetrahydropyranyl chloride (2.0 ml, 17 mmol) in 15 ml of diethyl ether was added via syringe to a freshly prepared solution of $KMn(CO)_5$ (ca. 20 mmol) in 15 ml of diethyl ether at −78°C under an atmosphere of argon. The solution was stirred at −78°C for 0.5 h in the absence of light, then warmed to 23°C for 1 h. The reaction was diluted with ethyl ether and quenched with 0.1 ml of water. The mixture was filtered through Celite and then concentrated in vacuo. The residue was purified by flash silica chromatography using a elution gradient from hexanes to 7% ethyl acetate/hexanes to give 4.6 g (97%) of 2-manganese pentacarbonyl tetrahydropyran (**31**) as a clear oil. A sample of **31** was crystallized from cold hexanes, filtered at −78°C to give a white solid, then recrystallized from pentanes at −20°C to give white crystals. M.p. 34–35°C; $R_f = 0.30$ (5% ethyl acetate/hexanes). IR (CCl_4): 2932, 2111, 2056, 2012, 1987. ^{1}H-NMR: (see Table 1). ^{13}C-NMR (50 MHz, C_6D_6): δ 211.97, 96.3, 85.5, 43.3, 21.9, 20.0. MS m/z (HR): Calc. for $C_{10}H_{10}MnO_6$ $(M^+ + H)$ 280.9857. Found 280.9858).



Scheme 9.



Scheme 10.

6.4. 2,3,4,6-Tetra-O-methyl- β-D-mannopyranosylmanganese pentacarbonyl (**34**) and 2,3,4,6-tetra-O-methyl-α-D-mannopyranosylmanganese pentacarbonyl (**35**)

A solution of 2,3,4,6-tetra-*O*-methyl-α-D-mannopyranosyl bromide (1.18 g, 1.95 mmol) in 15 ml of anhydrous Et_2O was added via syringe to a freshly prepared solution of $KMn(CO)_5$ (1.9 mmol) in 15 ml of anhydrous Et_2O at −78°C under argon. The solution was stirred in the dark at −78°C for 0.5 h, then warmed to 23°C for an additional 3 h. The reaction mixture was diluted with Et_2O and quenched with 0.1 ml of water. The mixture was dried over Na_2SO_4, filtered through a pad of Celite, and concentrated in vacuo. The residue was dissolved in 15 ml of anhydrous CH_2Cl_2 and transferred to Fisher–Porter apparatus. The system was evacuated (18 mmHg) and backfilled five times with carbon monoxide to 50 psi. The mixture was stirred in the dark for 4 days. The carbon monoxide was vented, and the solvent was evaporated in vacuo to give a yellow oil. The crude product was purified by flash chromatography eluting with a 5–25% gradient of EtOAc/hexanes to give 224 mg (28%) of 2,3,4,6-tetra-*O*-methyl-β-mannopyranosylmanganese pentacarbonyl (**34**) and 150 mg (17%) of 2,3,4,6-tetra-*O*-methyl-α-mannopyranosyl-1-acyl-manganese pentacarbonyl.

Decarbonylation of 2,3,4,6-tetra-*O*-methyl-α-mannopyranosyl-1-acylmanganese pentacarbonyl by heating to 62°C in benzene for 19 h gave 125 mg (89%) of 2,3,4,6-tetra-*O*-methyl-α-mannopyranosyl-manganese pentacarbonyl (**35**) as an oil. $R_f = 0.27$ (25% EtOAc/hexanes). IR (CCl_4): 2112, 2048, 2014, 1984. ^{1}H-NMR (400 MHz, C_6D_6): δ 5.04 (d, $J = 10.4$, 1H), 4.16 (t, $J = 7.06$, 1H), 3.76 (m, 2H), 3.50 (m, 2H), 3.48 (m, 1H), 3.19 (s, 3H), 3.14 (s, 3H), 3.10 (s, 3H), 3.08 (s, 3H). ^{13}C-NMR (100 MHz, C_6D_6): δ 212.0, 83.2, 76.7, 75.3, 75.1, 72.9, 70.6, 58.6, 58.2, 56.8, 54.4.

2,3,4,6-Tetra-*O*-methyl-β-mannopyranosylmanganese pentacarbonyl (**34**) was isolated as a yellow oil. $R_f = 0.30$ (25% EtOAc/hexanes). IR (CCl_4): 2160, 2056, 2012, 1987. ^{1}H-NMR (200 MHz, C_6D_6) δ 4.18 (d, $J = 1.0$, 1H), 3.64 (s, 3H), 3.58–3.62 (m, 3H), 3.48 (s, 3H), 3.27 (s, 1H), 3.18 (s, 3H), 3.15–3.17 (m, 3H). ^{13}C-NMR (50 MHz, C_6D_6) δ 211.9, 90.3, 85.0, 84.7, 81.7, 77.1, 72.6, 60.5, 60.5, 60.0, 58.0. MS (CI, m/z): (relative intensity) 415 ($M^+ + 1$, 1), 414 (M^+, 2), 359 (($M^+ + 1$) − 2 CO, 12), 343 (2), 327 (6), 313 (4), 274 (6), 219 (10), 187 (15), 157 (71), 143 (10, 125 (12), 101 (100).

2,3,4,6-Tetra-*O*-methyl-α-mannopyranosyl-1-acylmanganese pentacarbony was recrystallized from pentane to provide white crystals. M.p. 76–77°C; $R_f = 0.14$ (25% EtOAc/hexanes). IR (CCl_4): 2119, 2050, 2031, 2021, 1638. ^{1}H-NMR (400 MHz, C_6D_6) δ 4.12 (d, $J = 3.6$, 1H), 4.88 (t, $J = 3.4$, 1H), 3.67–3.77 (m, 2H), 3.49–3.53 (m, 2H), 3.34 (s, 3H), 3.27 (s, 3H), 3.19 (s, 3H), 3.17 (s, 3H), 3.1 (d, $J = 5.3$, 1H). ^{13}C-NMR (100 MHz, C_6D_6) δ 262.2, 209.4, 92.2, 81.6, 77.1, 77.0, 75.0, 72.4, 59.4, 59.0, 58.5, 57.6.

6.5. 2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl-1-acylmanganese pentacarbonyl (**36**)

A solution of glucopyranosylmanganese pentacarbonyl **22** (0.200 g, 0.278 mmol) in 15 ml of methylene chloride was sealed in a Fischer–Porter bottle with a gas inlet and pressure regulator. The solution in the bottle

was degassed three times via aspiration, backfilling with carbon monoxide. With an internal carbon monoxide pressure of 45 psi, the mixture was vigorously stirred at 20°C for 8 h shielded from light. The reaction mixture was opened to the atmosphere, concentrated under reduced pressure and the resulting oil purified by column chromatography eluting 5% ethyl acetate/hexanes to give 165 mg (80%) of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl-1-acylmanganese pentacarbonyl (**36**) as a clear oil. In addition, 30 mg (15%) of starting material **22** was recovered as a clear oil. Attempts to crystallize compound **36** were unsuccessful. $R_f = 0.27$ (10% ethyl acetate/hexanes). IR (CCl_4) 2118, 2053, 2024, 2000, 1650. ^{1}H-NMR (200 MHz, C_6D_6) δ 7.48–7.09 (m, 20H, Ar), 4.90 (AB q, $J_{AB} =$ 10.5 Hz, $\Delta\nu_{AB} =$ 28 Hz, 2H), 4.86 (s, 2H), 4.66 (AB q, $J_{AB} = 11.4$ Hz, $\Delta\nu_{AB} = 61$ Hz, 2H), 4.37 (AB q, $J_{AB} = 11.8$ Hz, $\Delta\nu_{AB} =$ 16 Hz, 2H), 3.80–3.65 (m, 5H), 3.52 (d, $J_{H1} = 8.6$ Hz, 1H), 3.50–3.44 (m, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 256.5, 209.6, 139.3, 139.1, 138.7, 128.5–127.5, 92.2, 87.0, 78.9, 78.4, 77.8, 75.4, 74.8, 73.6, 69.5. MS m/z (HR): Calc. for $C_{34}H_{36}O_5$ $[(M^+ + H) - Mn(CO)_5]$ 524.2547. Found 524.2563.

6.6. Methyl 2,6-anhydro-4,5,6,8-tetrakis-O-(phenylmethyl)-D-glycero-gulo-heptonate (37)

A suspension of glucopyranosylmanganese pentacarbonyl **22** (0.305 g, 0.507 mmol) and potassium carbonate (0.300 g, 2.17 mmol) in 10 ml of methyl alcohol was sealed in a Fischer–Porter bottle containing a gas inlet and pressure regulator. The reaction mixture in the bottle was degassed three times via aspiration, backfilling with carbon monoxide. With an internal carbon monoxide pressure to 45 psi, the mixture was stirred at 23°C for 20 h shielded from light. The clear solution, containing a white precipitate, was concentrated in vacuo and the resulting oil was diluted with ethyl acetate. This suspension was filtered through a pad of Celite, concentrated to a clear oil. The crude ester was purified by flash column chromatography eluting with 10% ethyl acetate/hexanes to give 270 mg (91%) of **37** as a white solid. Ester **37** was recrystallized from hexanes to give white needles. M.p. 71–72°C; $R_f = 0.30$ (25% ethyl acetate/hexanes). $[\alpha]_D^{23} = +12.0°$ (c 0.12, $CHCl_3$). IR (CCl_4) 1756. ^{1}H-NMR (200 MHz, C_6D_6): δ 7.34–7.10 (m, 20H), 4.83 (s, 2H), 4.73 (AB q, $J_{AB} =$ 11.3 Hz, $\Delta\nu_{AB} = 35$ Hz, 2H), 4.69 (AB q, $J_{AB} =$ 11.3 Hz, $\Delta\nu_{AB} = 46$ Hz, 2H), 4.38 (AB q, $J_{AB} =$ 12.1 Hz, $\Delta\nu_{AB} = 21$ Hz, 2H), 4.05–3.95 (m, 2H), 3.85–3.60 (m, 4H), 3.40–3.25 (m, 1H), 3.27 (s, 3H). ^{13}C-NMR (50 MHz, C_6D_6) δ 169.4, 139.4, 139.2, 139.0, 128.5–127.5, 86.8, 80.6, 80.4, 79.1, 78.4, 75.4, 75.0, 73.8, 69.4, 51.6. MS m/z (HR): Calc. for $C_{36}H_{39}O_7$ $(M^+ + H)$ 583.2697. Found 583.2696.

6.7. 2,6-Anhydro-3,4,5,7-tetrakis-O-(phenylmethyl)-D-glycero-gulo-heptonic acid amide (38)

A solution of glucopyranosylmanganese pentacarbonyl **22** (1.95 g, 2.71 mmol) and potassium carbonate (1.00 g, 7.21 mmol) in 10 ml of dry methanol was placed in a Fischer–Porter bottle. To this solution was added 20 ml of methanol previously saturated with anhydrous ammonia. The reaction vessel was stirred for 12 h under 40 psi of carbon monoxide in the absence of light. The yellow solution with a white precipitate was concentrated under reduced pressure to a paste, diluted with ethyl acetate, filtered through a pad of Celite and the filtrate was evaporated to a semi-solid. The crude amide was purified by column chromatography eluting with 33% ethyl acetate/hexanes to give a white solid. Compound **38** was recrystallized from hexanes/ethyl acetate to give 1.48 g (96%) as a white solid. M.p. 124–126°C; $R_f = 0.15$ (50% hexanes/ethyl acetate). $[\alpha]_D^{23} = +34.6°$ (c 0.55, $CHCl_3$). IR (CCl_4) 1703. ^{1}H-NMR (200 MHz, C_6D_6): δ 7.47 (d, $J = 7.2$ Hz, 2H), 7.34–7.07 (m, 18H), 5.77 (br s, 1H), 5.29 (br s, 1H), 4.92–4.50 (m, 6H), 4.38–4.20 (m, 3H), 3.83–3.53 (m, 5H), 3.47–3.26 (m, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 171.8, 138.5, 138.2, 128.3–127.2, 85.3, 80.1, 78.3, 78.0, 75.0, 74.5, 73.5, 69.6. MS m/z (HR): Calc. for $C_{35}H_{38}NO_7$ $(M^+ + H)$ 568.2700. Found 568.2699.

6.8. N-(phenylmethyl)-2,6-anhydro-3,4,5,7-tetrakis-O-(phenylmethyl)-D-glycero-gulo-heptonic acid amide (39)

A solution of glucopyranosylmanganese pentacarbonyl **22** (0.460 g, 0.640 mmol), benzyl amine (1.00 ml, 9.15 mmol) and potassium carbonate (1.00 g, 7.10 mmol) in 20 ml of dry methanol was placed in a Fischer–Porter bottle. The reaction vessel was stirred for 12 h under 45 psi of carbon monoxide in the absence of light. A yellow solution with a white precipitate was concentrated to a paste, diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was washed with 2 N HCl and brine then dried over sodium sulfate. The organic layer was filtered and concentrated in vacuo to give a clear oil. The crude amide was purified by column chromatography eluting with 25% ethyl acetate/hexanes to give 1.48 g (96%) of amide **39** as a white solid. Amide **39** was recrystallized from hexanes/ethyl acetate to give white crystals. M.p. 165–166°C; $R_f = 0.15$ (33% ethyl acetate/hexanes). IR (CCl_4) 1692: ^{1}H-NMR (200 MHz, C_6D_6) δ 7.50 (d, $J = 16.6$ Hz, 2H), 7.40 (d, $J = 6.6$ Hz, 2 H), 7.20–7.08 (m, 21H), 6.68 (t, $J = 5.8$ Hz, 1H), 4.91 (AB q, $J = 11.3$ Hz, $\Delta\nu_{AB} = 27$ Hz, 2H), 4.80 (AB q, $J = 10.8$ Hz, $\Delta\nu_{AB} = 33$ Hz, 2H), 4.68 (AB q, $J = 11.2$ Hz, $\Delta\nu_{AB} = 40$ Hz, 2H), 4.49–4.30 (m, 4H), 4.05–3.95 (m, 2H), 3.82–3.77 (m, 2H), 3.60 (br s, 2H), 3.55–3.45 (m, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 169.0, 138.3, 138.1,

138.0, 137.9, 128.6–127.4, 85.1, 80.0, 78.4, 77.6, 77.4, 74.9, 74.5, 74.4, 73.4, 68.9, 43.1. MS m/z (H/R): Calc. for $C_{42}H_{43}NO_6$ 657.3092. Found 657.2965.

6.9. Methyl 5,9-anhydro-2,3-dideoxy-6,7,8,10-tetrakis-O-(phenylmethyl)-D-glycero-D-gulo-dec-2-en-4-ulosonate (47)

A solution of glucopyranosylmanganese pentacarbonyl **22** (0.275, 0.383 mmol) and freshly distilled methyl acrylate (0.20 ml, 2.2 mmol) in 3 ml THF was placed in a plastic syringe and sealed with a luer lock cap. The syringe was placed in a high pressure apparatus and pressurized to 4500 bar. After 40 h, the pressure was released and the solution was concentrated in vacuo to give the crude manganacycle **43** as a thick red oil. The unstable manganacycle was used in the next step without further purification. The manganacycle **43** was diluted with 20 ml acetonitrile and 0.5 ml of water. This solution was stirred open to the atmosphere while subjected to photo irradiation (320 nm) for 4 h. Internal temperature of the reaction mixture reached 60–65°C due to the light source. The solution became dark with a brown precipitate which was filtered with Celite from the reaction mixture. The filtrate was concentrated in vacuo and the resulting residue was purified by column chromatography eluting with 5% ethyl acetate/hexanes to give 163 mg (67%) of methyl ester **47** as a white solid. Attempts to recrystallize compound **47** were unsuccessful. $R_f = 0.38$ (25% ethyl acetate/hexanes). IR (CCl_4): 1733. ^{1}H-NMR (200 MHz, C_6D_6): δ 7.52 (d, $J = 15.9$ Hz, 1H), 7.38–7.06 (m, 20H), 6.92 (d, $J = 15.9$ Hz, 1H), 4.87 (s, 2H), 4.73 (AB q, $J_{AB} = 8.9$ Hz, $\Delta\nu_{AB} = 16$ Hz, 2H), 4.65 (AB q, $J_{AB} = 11.1$ Hz, $\Delta\nu_{AB} = 16$ Hz, 2H), 4.42 (AB q, $J_{AB} = 12.2$ Hz, $\Delta\nu_{AB} = 19$ Hz, 2H), 3.85 (d, $J = 9.2$ Hz, 1H), 3.80–3.54 (m, 5H), 3.37–3.27 (m, 1H), 3.31 (s, 3H). ^{13}C-NMR (50 MHz, C_6D_6) δ 194.2, 165.5, 139.2, 139.0, 138.8, 138.3, 136.49, 131.7, 128.5–127.5, 86.7, 82.4, 82.4, 79.7, 78.9, 77.9, 75.4, 75.0, 74.8, 73.5, 68.9, 51.6.

6.10. Methyl 5,9-anhydro-2,3-dideoxy-6,7,8,10-tetrakis-O-(phenylmethyl)-D-glycero-D-gulo-deculosonate pyrimidone (49)

A solution of ketone **48** (55 mg, 86 mmol) in 4 ml of 100% ethyl alcohol and 0.1 ml of glacial acetic acid was treated with hydrazine (50 ml, 1.0 mmol) under an atmosphere of nitrogen. The solution was stirred and heated at reflux for 1 h, then cooled to 23°C for 1 h. The solution was poured into 2 N HCl and extracted thoroughly with ethyl acetate. The organic layers were combined and dried over sodium sulfate, then concentrated in vacuo. The resulting residue was purified by column chromatography eluting with 10% ethyl acetate/hexanes to give 46 mg (86%) of dihydropyridazine **49** as a white solid. Attempts to recrystallize compound **49** were unsuccessful. $R_f = 0.15$ (33% ethyl acetate/hexanes). IR (CCl_4) 3431, 1700, 1650, 1495. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.62 (br s, 1H), 7.37–7.14 (m, 20H), 4.93 (s, 2H), 4.87–4.78 (m, 2H), 4.62–4.54 (m, 4H), 3.92 (d, $J = 9.7$ Hz, 1H), 3.78–3.50 (m, 6H), 2.62–2.45 (m, 1H), 2.40–2.25 (m, 2H), 2.05–1.85 (m, 1H). ^{13}C-NMR (50 MHz, C_6D_6) δ 167.0, 155.8, 139.4, 139.1, 138.8, 138.8, 128.5–127.3, 87.4, 81.2, 79.3, 78.9, 78.3, 75.6, 75.0, 74.5, 73.5, 69.2, 26.1, 21.0. MS m/z (relative intensity): 621 [($M^+ + 1$) 18], 529 (40), 515 (46), 424 (71), 315 (14), 253 (28), 181 (100), 149 (42).

6.11. Dihydropyrazole (51)

Sugar ester **47** (71.0 mg, 0.11 mmol) was dissolved in 4 ml of absolute ethanol followed by hydrazine monohydrate (20 μl, 0.41 mmol) and 2 drops of glacial acetic acid. The reaction was stirred at room temperature (23°C) for 25 h. The reaction mixture was concentrated in vacuo and dissolved in 5 ml EtOAc then washed with 2 N HCl followed by brine. The organic layer was concentrated in vacuo and chromatographed with 25% EtOAc/hexanes to give 59 mg (81%) of dihydropyrazole **51** as a white solid in a 2:1 diastereomeric mixture. Attempts to recrystallize compound **51** were unsuccessful. $R_f = 0.10$ (33% EtOAc/hexanes). IR (CCl_4): 3350, 1743. ^{1}H-NMR (200 MHz, C_6D_6): δ 7.41–6.92 (m, 20 H), 5.10–4.78 (m, 4 H), 4.71–4.59 (m, 2H), 4.48–4.23 (m, 2 H), 3.85–3.47 (m, 8 H), 3.38–3.17 (m, 4 H), 3.09 (s, 1H), 3.01 (s, 3 H). ^{13}C-NMR (50 MHz, C_6D_6) δ 139.5, 139.2, 139.0, 128.5, 128.0, 127.5, 87.3, 87.1, 86.2, 80.2, 79.6, 79.4, 78.3, 78.1, 77.5, 75.5, 75.1, 74.9, 74.8, 73.9, 73.6, 70.2, 60.3, 51.8. MS m/z (H/R): Calc. for $C_{39}H_{42}N_2O_7$ 663.3072. Found 663.2945.

6.12. Phenylsulfone (52) and furanone (55)

A solution of glucopyranosylmanganese pentacarbonyl **22** (0.460 g, 0.640 mmol) and phenyl vinyl sulfone (0.20 g, 1.2 mmol) in 3 ml THF was placed in a plastic syringe and sealed with a luer lock cap. The syringe was placed in a high pressure apparatus and pressurized to 4500 bar. After 40 h, the pressure was released and the solution was concentrated to give the crude manganacycle **44** as a thick red oil. The unstable manganacycle was used in the next step without further purification. A solution of crude manganacycle **44** (0.50 g, 0.56 mmol) in 15.0 ml of acetonitrile and 0.15 ml water was degassed by a series of freeze/vacuum/thaw cycles. The solution was stirred under partial vacuum while being subjected to photo irradiation (320 nm) for 12 h. The internal temperature of the reaction mixture reached 60–65°C due to the light source. As the clear yellow solution was opened to the air, the reaction mixture became dark and eventually formed a red–

brown precipitate (an oxidized manganese by-product). After 1 h the suspension was filtered, concentrated in vacuo, and the resulting residue was purified by column chromatography eluting with 5% ethyl acetate/hexanes to give 0.262 g (65%) of butenolide **55** as a white solid and 139 mg (35%) of keto-sulfone **52** as a white solid. Sulfone **52** was recrystallized from hexanes to give white crystals. $R_f = 0.10$ (25% ethyl acetate/hexanes). IR (CCl_4): 1738, 1325, 1156. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.90–7.85 (m, 2H), 7.62–7.45 (m, 3H), 7.30–7.10 (m, 20H), 4.78 (s, 2H), 4.75–4.50 (m, 6H), 4.33–4.15 (m, 7H), 3.30–3.12 (m, 2H), 3.10–2.95 (m, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 200.3, 139.3–139.3, 133.6, 129.3, 128.4–127.7, 86.2, 82.6, 79.3, 78.7, 78.0, 75.3, 74.8, 74.5, 73.7, 69.4, 50.4, 32.6. MS m/z (HR): Calc. for $C_{43}H_{44}O_8S$ 720.2757. Found 720.2948.

Furanone **55** was recrystallized from hexanes to give white crystals. $R_f = 0.15$ (25% ethyl acetate/hexanes). IR (CCl_4): 1766, 1495. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.27–7.10 (m, 20H), 6.77 (dd, $J = 1.4$, 5.7 Hz, 1H), 5.92 (dd $J = 1.4$, 5.8 Hz, 1H), 5.11 (d, $J = 1.4$ Hz, 1H), 4.95–4.72 (m, 6H), 4.53 (dd, $J = 4.2$, 10.2 Hz, 2H), 4.43 (s, 2H), 3.70–3.52 (m, 4H), 3.41–3.30 (m, 1H). ^{13}C-NMR (50 MHz, C_6D_6): δ 171.8, 151.3, 139.2, 139.2, 138.4, 128.4–127.6, 122.2, 87.5, 82.2, 79.8, 78.8, 78.3, 77.8, 75.4, 74.9, 74.2, 73.7, 69.1. MS m/z (HR): Calc. for $C_{38}H_{37}O_7$ 605.2540. Found 605.2414. Calc. for $C_{31}H_{31}O_7$ (M–Bn) 515.2070. Found 515.2011.

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