signals were evident, indicating that the species were not interconverted rapidly on the NMR time scale and that CO does not rapidly coordinate to the alkyliron(III) porphyrin. Pyrrole deuteron signals for the CO adducts of (TPP)Fe-ethyl and (TPP)-Fe-neopentyl complexes were at -8.0 and -7.1 ppm, respectively. The (TPP)Fe-norbornyl complex was resistant to CO insertion under the conditions cited above. Absence of splitting or asymmetry of the signal rules out alkyl group migration to the pyrrole nitrogen sites. The upfield position and relatively narrow line width for the new pyrrole signal are indicative of a low-spin iron(III) tetraphenylporphyrin product. Electron spin resonance spectra at 5 K confirm the low-spin character with g values of 2.56, 2.38, and 1.88.

The proton NMR spectrum of the product formed between (TPP)FeBu and CO revealed two new signals at 18.6 and -1.3 ppm approximately one-fourth the intensity of the pyrrole signal at -8.2 ppm. On the basis of comparisons with the acetyl and butyryl analogues, these signals are assigned to the β and γ protons of $-C(O)CH_2CH_2CH_2CH_3$, respectively (the α-CH_2 signal is broadened beyond detection, and the $-CH_3$ signal overlaps with diamagnetic region signals). The red solution persists for hours under anaerobic conditions but is otherwise highly oxygen and moisture sensitive. The green (TPP)Fe-O-Fe(TPP) is formed upon exposure to the atmosphere. Addition of HCl vapor to the red CO adduct of (TPP)FeBu elicited conversion to the parent (TPP)FeCl species.

Following addition of CO to (TPP)FeBu, IR spectra (toluene solvent) revealed appearance of a new solvent sensitive band at 1817 cm^{-1} (1765 cm^{-1} with ^{13}CO). These overall results are suggestive of CO insertion into the Fe-C bond of the original alkyl complex, with subsequent formation of a novel acyl-iron(III) porphyrin complex. Acyliron(III) porphyrin complexes have not

$$(TPP)Fe\text{-}CH_2(CH_2)_2CH_3 + CO \rightarrow (TPP)Fe\text{-}C(=O)(CH_2)_3CH_3$$

been reported,[10] and hence an independent synthetic route was devised. Addition of butyryl chloride to the iron(I) tetraphenylporphyrin anion[11] produced a small amount of the species with a -8.2 ppm pyrrole peak. However, the putative acyliron(III) product was prepared as the predominant species by addition of the acyl chloride to the corresponding iron("0") tetraphenylporphyrin dianion with subsequent iodine oxidation of the iron(II) derivative to an iron(III) complex spectroscopically identical to the CO insertion product.

The CO insertion reaction is first-order in CO pressure at pressures less than 1 atm and first-order in alkyliron(III) porphyrin. Among mechanistic speculations is the possibility for a CO-assisted homolytic scission of the iron-alkyl bond with attack of the immediate Fe-CO product by a caged alkyl radical. This process would account for appearance of significant amounts of (TPP)Fe(CO) as a byproduct.

A parallel insertion reaction with CO_2 would be expected to produce a carboxylate complex, and this is indeed confirmed on the basis of spectroscopic comparisons with known carboxylato-iron(III) porphyrin derivatives. Following addition of CO_2 to a benzene solution of (TPP)FeBu, the red solution with a pyrrole deuteron signal at -17.2 ppm was converted over a period of hours to a green species with a pyrrole deuteron signal at 80 ppm. The proton NMR spectrum of this complex revealed meta-phenyl signals at 12.7 and 11.7 ppm as expected for a high-spin (TPP)$Fe^{(III)}$ carboxylate complex.[12] A broad signal at 20.7 ppm is assigned to a β-CH_2 group of the carboxylate ligand on the basis of a recent spectroscopic study of carboxylate complexes.[13] The green solution exhibited optical spectral bands at 410, 572, and 610 nm, consistent with spectra observed for oxygen-ligated (TPP)$Fe^{(III)}$ complexes. The net reaction observed for CO_2 insertion is thus summarized by

$$(TPP)Fe\text{-}CH_2(CH_2)_2CH_3 + CO_2 \rightarrow (TPP)Fe\text{-}OC(=O)(CH_2)_3CH_3$$

The reactivity of alkyliron(III) porphyrins (and possibly the aryl analogues) suggests that a large number of new coordination complexes are feasible through addition of other ligand types. Investigation of the low-spin iron(III) derivatives is also of interest in terms of developing the organometallic chemistry of paramagnetic species.

Acknowledgment. Support from National Science Foundation Grants CHE 83-17451 and CHE 87-05703 is gratefully acknowledged.

(10) The acetyl cobalt(III) porphyrin derivative has been prepared through use of a Grignard reagent: Clarke, D. A.; Dolphin, D.; Grigg, R.; Johnson, A. W.; Pinnock, H. A. *J. Chem. Soc. C* **1968**, 881.

(11) Hickman, D. L.; Shirazi, A.; Goff, H. M. *Inorg. Chem.* **1985**, *24*, 563.

(12) Oumous, H.; Lecomte, C.; Protas, J.; Cocolios, P.; Guilard, R. *Polyhedron* **1984**, *3*, 651.

(13) Arafa, I. M.; Goff, H. M.; David, S. S.; Murch, B. P.; Que, L., Jr. *Inorg. Chem.* **1987**, *26*, 2779.

Preparation of Complex Aminoglycosides: A New Strategy

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Aminoglycosides are widely distributed in nature and are found in a large variety of biologically important molecules. A few examples of these are aminopolysaccharides, such as blood group determinants and antigenic determinants on cell surfaces,[1] aminoglycoside antibiotics,[2] glycoproteins, glycolipids,[3] and nucleoside antibiotics (i.e., tunicamycin).[4] In the past, synthesis of these molecules has generally required two separate strategies, one for the preparation of the appropriate aminosugar and another for the glycosidation of this sugar.

Recently, we have described a new mild, highly stereoselective and efficient method for the preparation of aminosugars which involve the cycloaddition of an azodicarboxylate onto a glycal.[5] Herein, we report that the cycloadducts obtained by this reaction are powerful and versatile glycosylating agents and can be used to prepare a variety of complex glycosides. This allows both the aminosugar and the glycoside preparation to be combined in a single, mild, simple, and efficient strategy for the first time.

A wide variety of glycals smoothly undergoes a [4 + 2] cycloaddition with dibenzyl azodicarboxylate to give dihydrooxadiazines of the general formula **1**. Previously, we have described this reaction with several furanoid glycals[5] and since have found that this reaction proceeds well with all furanoid and pyranoid glycals attempted, with the exception of those bearing an allylic acyloxy function (i.e., R = Ac, Scheme I). This work will be described in detail at a later date.

In our initial work, we noted that when the cycloadducts were treated with *p*-TsOH in methanol, they underwent stereospecific opening at C-1 with inversion of stereochemistry. Therefore, it was felt that these dihydrooxadiazines may provide entries to more complex aminoglycosides as well as to the parent aminosugar. However, the analogy, while very tempting, is not direct since the

(1) Kabat, E. A. In *Blood and Tissue Antigens*; Aminoff, D., Ed.; Academic: New York, 1970; p 187.

(2) Umezawa, S. In *Advances in Carbohydrate Chemistry and Biochemistry*; Tipson, R. S., Derek Horton, D., Eds.; Academic: London, 1974; pp 111-182.

(3) Watkins, W. M. In *Glycoproteins*; Gottschalk, A., Ed.; Elsevier: Amsterdam, 1972; p 830.

(4) Fukuda, Y.; Kitasato, H.; Sasai, H.; Suami, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 880-886.

(5) Fitzsimmons, B. J.; Leblanc, Y.; Rokach, J. *J. Am. Chem. Soc.* **1987**, *109*, 285-286.

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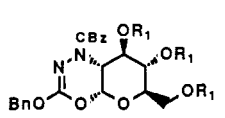
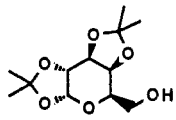
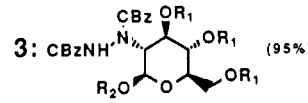
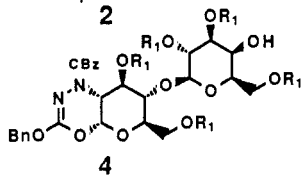
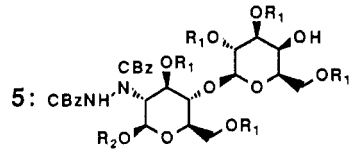
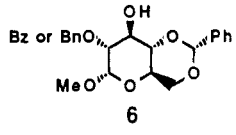
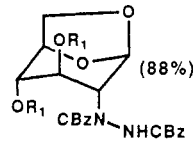
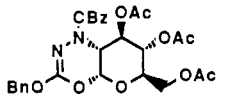
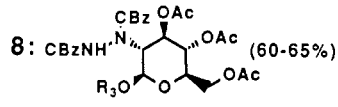
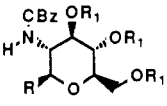
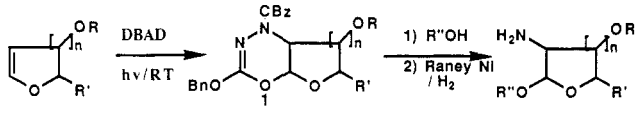
Table I

cycloadduct	nucleophile	conditions	glycoside (yield)
 R_1=TBDMSi **2**	 $=R_2OH$	$TsOH(cat.)/CH_2Cl_2$ R.T. 10 min.	**3**:  (95%)
 **4**	R_2OH	$TsOH(cat.)/CH_2Cl_2$ R.T. 10 min. (46%) $BF_3.Et_2O$ -40°C (82%)	**5**: 
2	 **6**	$TsOH/ CH_2Cl_2$ $BF_3.Et_2O$ -40°C	COMPLEX MIXTURE **7**:  (88%)
	**6**:=R_3OH	$BF_3.Et_2O$ -40°C	**8**:  (60-65%)
2	DIHYDROCHOLESTEROL=R_5OH	$TsOH(cat.)$ CH_2Cl_2	**9**: R= OR_5 (96%)
	ACETIC ACID	$TsOH(cat.)/$ACETIC ANHYDRIDE	**10**: R= OAc (90%)
	H	$NaBHCN_3/ZnI_2,CH_2Cl_2$	**11a**: R=H **11b**: R=D (84%) 

Scheme I



alcohol in these cases was methanol and was used as solvent. Therefore, the question remained whether the promise of this reaction could be realized with close to equimolar amounts of complex primary and secondary alcohols and the cycloadducts.

Treatment of the dihydrooxadiazine **2**, obtained from glucal, with 1.2 equiv of diacetone galactose in dichloromethane with a catalytic amount of *p*-TsOH gave the disaccharide **3** in 71% yield. Similarly, the disaccharide cycloadduct **4**, from lactal,[6] gave the trisaccharide **5**, however in only a 46% yield. The trisaccharide **5** differs only in its protecting groups to one prepared by Lemieux et al. in his blood group determinant studies.[7]

Next, we turned our attention to the considerably more challenging case of a secondary carbohydrate alcohol, choosing the C3 hydroxyl of the glucose derivative **6** as our example.

Treatment of the cycloadduct **2** with the alcohol **6** and *p*-TsOH in dichloromethane gave a complex mixture of products; therefore, an alternative activator of the dihydrooxadiazine was sought. Treatment of the cycloadduct **2** in the presence of the alcohol **6** (1.5 equiv) at −40 °C with BF_3·Et_2O clearly generated a new product. However, this material was not the result of the desired intermolecular reaction but rather of internal attack by the C6 oxygen to give the 1,6-anhydrosugar **7**. To circumvent this problem, the C6 oxygen was rendered less nucleophilic by changing the silyl-protecting groups to acetates. In this case, coupling of this cycloadduct and the secondary alcohol **6** occurs in good yield to give the disaccharide **8**.

Since the formation of the 1,6-anhydrosugar requires a conformational change, it was felt that the lactal cycloadduct **4** may have a higher barrier to this process relative to the glucal cycloadduct **2**. Therefore, in an attempt to improve the yield of the coupling reaction in this case, the cycloadduct **4** was treated with BF_3·Et_2O and diacetone galactose at −40 °C for 4 h resulting in an 82% yield of the trisaccharide **5**.

With the ability to prepare oligosaccharides established, we investigated other candidates for the nucleophilic opening of the dihydrooxadiazines. Treatment of the cycloadduct **2** and dihydrocholesterol (1.2 equiv) in dichloromethane with *p*-TsOH gave the coupled product **9** in excellent yield. Next, we turned our attention to acetate as a nucleophile and found that dissolution of the cycloadduct **2** in acetic anhydride/acetic acid/*p*-TsOH[8] led to a good yield of the anomeric acetate **10**. Finally, we attempted the opening with hydride to give the 1,5-anhydrosugar. Addition of the cycloadduct to a mixture of $NaBHCN_3$ and ZnI_2 in dichloromethane gave an excellent yield of the 1,5-anhydrosugar **11a**; moreover, when the reaction was repeated with sodium cyanoborodeuteride, the deuterium was introduced stereospecifically to give **11b**.

The cycloadduct opening products could be converted in good yield to their corresponding amines by hydrogenation over Ra–Ni as we have reported previously.[5]

In summary, the [4 + 2] cycloaddition of azodicarboxylates and carbohydrate glycals produces a powerful glycosylating agent. These cycloadducts can be utilized in the preparation of aminopolysaccharides and other complex aminoglycosides thus allowing

(6) Haworth, W. H.; Hirst, E. L.; Plant, M. T.; Reynolds, R. J. W. *J. Chem. Soc.* **1930**, 2644–2653.

(7) (a) Lemieux, R. U.; Abbas, S. Z.; Burzynska, M. H.; Ratcliffe, R. M. *Can. J. Chem.* **1982**, *60*, 63–67. (b) Lemieux, R. U.; Burzynska, M. H. *Can. J. Chem.* **1982**, *60*, 76–80. The trisaccharide **5** was converted to the *N*-phthalimido peracetyl derivative (compound **18** in ref 7a). The physical and spectral characteristics of this compound were in agreement with those reported: mp 202–203 °C (ethanol), $[\alpha]^{22}_D$ − 19.4 (*c* 1.0, $CHCl_3$), lit. mp 201–202 °C (ethanol), $[\alpha]^{29}_D$ −19.6 (*c* 0.8, $CHCl_3$).

(8) Micheel, F.; Kochling, H. *Chem. Ber.* **1958**, *91*, 673–676.

(9) All new compounds cited in this article gave satisfactory elemental analyses and spectral data. The ^1H NMR spectra of the glycoside were recorded at 80 °C in C_6D_6 due to broad signals at lower temperatures.

these important molecules to be prepared simply and stereospecifically. Also this method yields the nitrogen function in a protected form and allows the preparation of the hydrazine analogues. In addition, the dihydrooxadiazine intermediates show the promise of stereoselective opening with non-oxygen-based nucleophiles. Further studies on the scope of the reactions of these cycloadducts will be reported in due course.

Acknowledgment. We thank Dr. M. Bernstein for performing variable temperature—^{1}H NMR on the glycosides. N.C. thanks NSERC (Canada) for an Undergraduate Student Research Award.

A Metal-Catalyzed Cyclization of Enallenes

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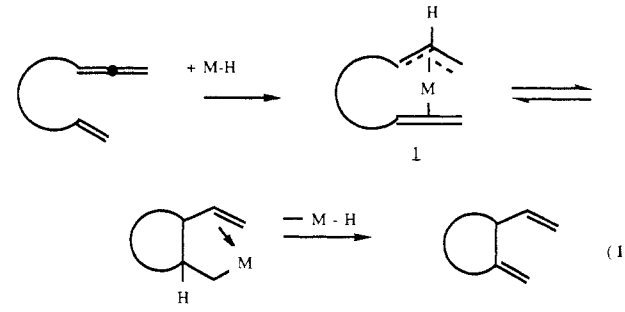
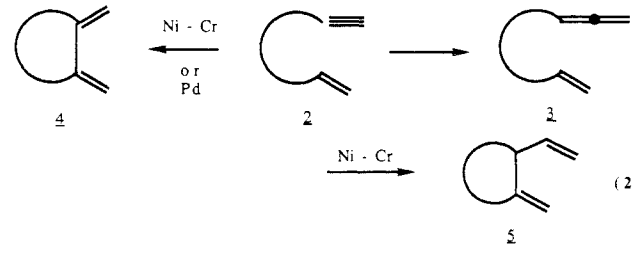
The development of chemical processes which involve a set of reactants that corresponds exactly to the empirical formula of the desired product avoids the development of chemical wastes that require disposal. Such a process for ring construction involves isomerizing an acyclic system. Cyclizations involving catalytic intramolecular carbametalations represent a type of reaction that meets such a goal.[1-6] The greatest success has focussed upon the acetylenic linkage. We wish to report that allenes can serve as an excellent functional group for cyclizations via isomerizations with use of a novel nickel–chromium bimetallic catalyst.[5,7]

The concept for the cyclization derives from our postulating that a metal hydride,[8] which was involved in the isomerization of enynes to five- and six-membered rings with a nickel–chromium catalyst,[5] may initiate the sequence of events outlined in eq 1.[7,9-11]



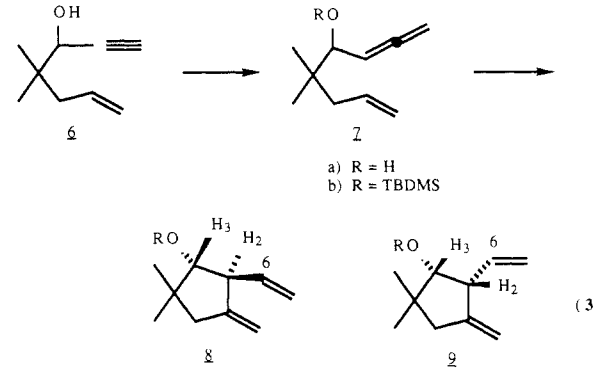
(1)

The existence of such a process would significantly extend the value of the catalytic intramolecular carbametalation. As shown in eq 2, the enynes **2**, which are easily transformed into the enallenes **3**,[12] then serve as common precursors to either 1,3-dienes like **4**[4,5] or 1,4-dienes represented by **5**.



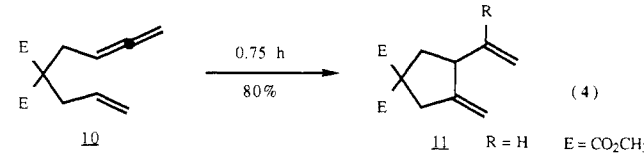
(2)

To probe the process, the allene **7a**, easily available from the corresponding acetylene **6** [$(CH_2O)_n$, $(i\text{-}C_3H_7)_2NH$, CuBr, dioxane, reflux, 59%], was exposed to 10 mol% of (*p*-diphenylphosphinopolystyrene)nickel dichloride and 30 mol% chromous chloride in 4:1 THF–ethanol at ambient temperature (eq 3).



(3)

These standard conditions effected cyclization to a 3.4:1 mixture of **8a**[13] and **9a**[13] in 55% isolated yield. Upon the basis of both proton coupling constants ($J_{2,3}$ = 10.2 Hz for **8a** and 5.5 Hz for **9a**) and ^{13}C NMR data (δ_{C_6} = 138.97 for **8a** and 136.30 for **9a**), the major product is assigned as trans. Performing the same reaction on the *tert*-butyldimethylsilyl ether **7b** increases the yield to 78% and the diastereoselectivity to >99:1 by capillary VPC.



(4)

(1) For stoichiometric intramolecular carbametalations of enynes, see: Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788. Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917; Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. Negishi, E. Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568. For reviews, see: Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65. Yasuda, H.; Nakamura, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 723.

(2) For metalloene reactions and other main group intramolecular carbametalations, see: Oppolzer, W.; Schneider, P. *Helv. Chim. Acta* **1986**, *69*, 1817 and earlier references in the series. Felkin, H.; Kwart, L. D.; Swierczewski, G.; Umpleby, J. D. *J. Chem. Soc., Chem. Commun.* **1975**, 242. Courtois, G.; Masson, A.; Miginiac, L. *C. R. Acad. Sci. Paris Ser. C* **1978**, *286*, 265. Jousseaume, B.; Douboudin, J. G. *Synth. Commun.* **1979**, *9*, 53. Crandall, J. K.; Battioni, P.; Wehlacz, J. T.; Bindra, R. *J. Am. Chem. Soc.* **1975**, *97*, 7171. Hill, E. A. *J. Organomet. Chem.* **1975**, *91*, 123. Richey, H. G.; Rothman, A. M. *Tetrahedron Lett.* **1968**, 1457.

(3) For Pd catalyzed intramolecular additions of allyl acetates to olefins, see: Oppolzer, W.; Gaudin, J.-M. *Helv. Chim. Acta* **1987**, *70*, 1477. Trost, B. M.; Luengo, J., to be published.

(4) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781. Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887. Trost, B. M.; Chen, S. F. *J. Am. Chem. Soc.* **1986**, *108*, 6053.

(5) (a) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 5268. (b) Also, see: Bogdanovic, B. *Adv. Organomet. Chem.* **1979**, *17*, 105.

(6) Takacs, J. M.; Anderson, L. G.; Creswell, M. W.; Takacs, B. E. *Tetrahedron Lett.* **1987**, *28*, 5627. Takacs, J. M.; Anderson, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 2200.

(7) Surprisingly, there has been little work involving nickel-catalyzed reactions of allenes. See: Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: 1975; Vol II, Chapter 2. Jolly, P. W. *Comp. Organomet. Chem.* **1982**, *8*, 649.

(8) Jolly, P. W. *Comp. Organomet. Chem.* **1982**, *6*, 37.

(9) Jolly, P. W. *Comp. Organomet. Chem.* **1982**, *8*, 671.

(10) dePasquale, R. J. *J. Organomet. Chem.* **1971**, *32*, 381. Otsuka, S.; Tani, K.; Yamagata, T. *J. Chem. Soc., Dalton Trans.* **1973**, 2491. Jolly, P. W.; Kruger, C.; Salz, R.; Sckutowski, J. C. *J. Organomet. Chem.* **1979**, *165*, C39. Hene, B.; Jolly, P. W.; Salz, R.; Stobbe, S.; Wilke, G.; Benn, R.; Mynott, R.; Seevogel, K.; Goddard, R.; Kruger, C. *J. Organomet. Chem.* **1980**, *191*, 449.

(11) For addition of a π-allylnickel to norbornene, see: Gallazzi, M.-C.; Porri, L.; Vitulli, G. *J. Organomet. Chem.* **1975**, *97*, 131. The cooligomerization of dienes with olefins presumably involves such a process. See: ref 5b, 9, and Jolly et al. (Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: 1975; Vol II, Chapter 1, pp 26–39).

(12) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 747. We have found that significant improvement in our yields resulted when (1) the temperature was maintained at 70 °C for 1 h before raising it to reflux and (2) approximately 0.5 mol% of BHT was added.

(13) This compound has been fully characterized spectroscopically, and elemental composition has been established by high resolution mass spectroscopy and/or combustion analysis.

0002-7863/88/1510-5231$01.50/0