Tetrahedron Letters, Vol.31, No.44, pp 6277-6280, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

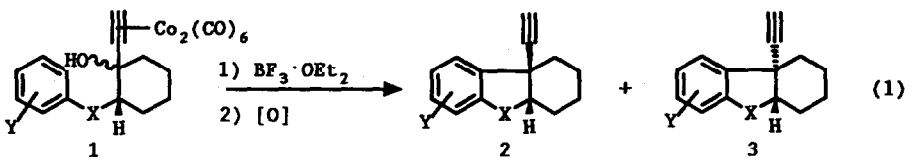
USE OF DICOBALT HEXACARBONYL-STABILIZED PROPARGYL CATIONS IN INTRAMOLECULAR FRIEDEL-CRAFTS ALKYLATIONS[1]

David D. Grove,* Frank Miskevich, Chase C. Smith, and James R. Corte

Department of Chemistry, Eckerd College
St. Petersburg, FL 33711

Abstract: *Cis*-9a-ethynyl-1,2,3,4,4a,9a-hexahydro-9*H*-fluorenes and the corresponding dibenzofurans have been prepared by a stereoconvergent, intramolecular Friedel-Crafts alkylation involving dicobalt hexacarbonyl-stabilized carbocations.

As part of a program to develop new synthetic routes to naturally occurring alkaloids, we have been investigating the use of dicobalt hexacarbonyl-stabilized carbocations in intramolecular Friedel-Crafts alkylations, eq.1.[2] This chemistry allows the facile assembly of tricyclic



X = CH_2, O
Y = H, OCH_3

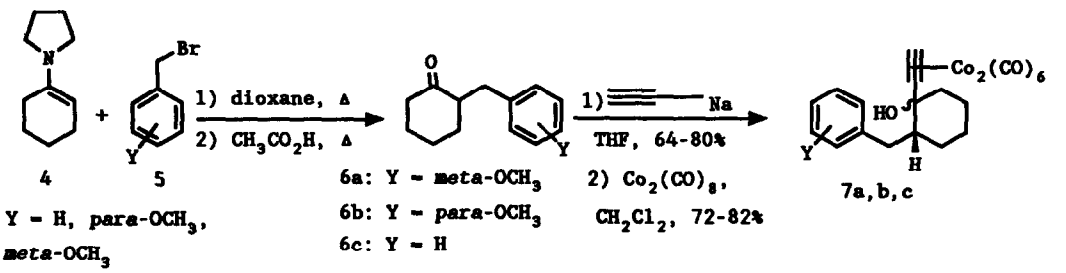
ring systems with concomitant generation of a quaternary, benzylic carbon atom, to which is attached the synthetically versatile ethyne group. The important issue to be addressed here is one of stereochemistry. Namely, will cyclization of diastereomeric alcohols **1** be a stereospecific or a stereoconvergent process?

Since carbon-oxygen bond heterolysis in dicobalt hexacarbonyl-complexed propargyl alcohols occurs with backside participation of cobalt,[3] and subsequent nucleophilic attack occurs in a stereospecific manner, i.e., anti to cobalt,[3] an intramolecular Friedel-Crafts alkylation involving **1**, could result in a mixture of *cis* and *trans*-fused products (**2** and **3**, eq.1). Schreiber has shown[3] however, that the fluxional nature of dicobalt hexacarbonyl-stabilized cations results in exposure of both faces to nucleophilic attack. Thus, if intramolecular arylation of the cation is slow compared to the migratory processes responsible for cation stereomutation, the *cis* isomer **2** should be formed exclusively, as is the case with

related, uncomplexed cations.[4] We have examined four simple systems to answer this stereochemical question and to define any regiochemical or electronic constraints related to the chemistry depicted in eq.1.

Initial efforts were aimed at the preparation of the methylene-linked (eq. 1, X = CH_2) cyclization substrates **7a,b,c** (Scheme 1). Addition of

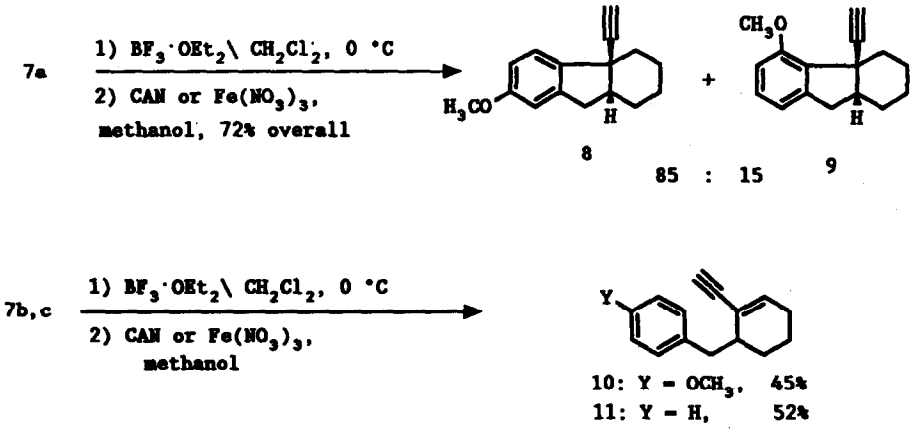
Scheme 1



sodium acetylide to ketones **6a,b,c**[5,6] afforded the corresponding propargyl alcohols in acceptable yield. Each alcohol was obtained as ca. 7:3 mixture of diastereomers as determined by ^1H NMR. Reaction of the alcohols with dicobalt octacarbonyl[2] in CH_2Cl_2 furnished the dicobalt hexacarbonyl-complexed alcohols **7a,b,c**[6] in good yield.

Reaction of alcohol **7a** with $BF_3 \cdot OEt_2$ in CH_2Cl_2 at 0 °C and then immediate decomplexation, using either ceric ammonium nitrate[7] (CAN) or $Fe(NO_3)_3$,[8] gave a 72% yield of the ethynylhexahydrofluorenes **8**[6] and **9**[6] in a 85:15 ratio (Scheme 2). While it was difficult at this point to ascertain

Scheme 2

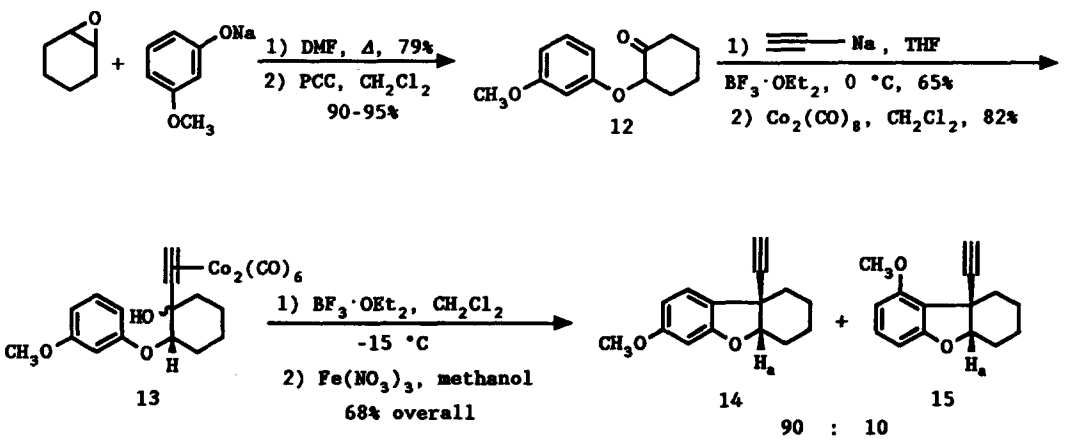


whether the *cis* or the *trans* product had been formed (vide infra), it was apparent from the ^1H NMR spectrum that a single stereoisomer had been produced. Admixture of **7b,c** with two equivalents of $BF_3 \cdot OEt_2$ in CH_2Cl_2 at

0 °C followed by decomplexation gave predominantly (>90% by 300 MHz ^{1}H NMR) the less-substituted enynes **10**[6] and **11**[6] in 45% and 52% yields respectively. In these two cases, the aromatic ring is not resonance-activated at the position where ring closure is expected to occur and elimination to the cobalt-complexed enynes occurs instead. The production of the less-substituted enynes is apparently due to a *cis* steric interaction[9] between the bulky dicobalt hexacarbonyl moiety and the benzyl group in the more-substituted, cobalt-complexed enyne product.[10]

The oxygen-linked substrate (eq.1, X = O) was prepared as shown in Scheme 3. Reaction of the sodium anion of 3-methoxyphenol with cyclohexene

Scheme 3



oxide in hot DMF followed by PCC[11] oxidation gave ketone **12**. Addition of sodium acetylide to a solution of **12** and $BF_3{\cdot}OEt_2$[12] in THF at 0 °C followed by neutralization gave the desired alcohol (ca. 6:4 mixture of diastereomers) which was then converted to dicobalt hexacarbonyl complex **13**.[6] Reaction of **13** with two equivalents of $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at -15 °C followed by decomplexation [$Fe(NO_3)_3$] gave, after chromatography (40:1 pet.ether:ether), a mixture of ethynylhexahydrodibenzofurans **14**[6] and **15**[6] in 68% yield and a 90:10 ratio (HPLC). Conversion of the triple bond in **14**/**15** to an ethyl group[13] allowed NOEDS studies to be performed; mutual enhancements were observed between H_a and the protons of the ethyl group. These studies confirm the *cis* stereochemistry shown for **14**/**15** and also support the stereochemical assignment intimated in Scheme 2 for **8** and **9**.

We have demonstrated that dicobalt hexacarbonyl-stabilized propargyl cations can be used in intramolecular Friedel-Crafts alkylations to generate useful tricyclic ring systems. Importantly, it has been shown that this reaction is stereoconvergent, yielding solely *cis*-fused products, and

regioselective. The electronic requirement of resonance donation of electron density to the site of cyclization may limit the potential usefulness of the process. Applications of this chemistry to the synthesis of alkaloids is currently being pursued in our laboratory.

References and Notes.

(1) Presented in part by C.C.S. at the 3rd Annual Conference on Undergraduate Research, April 27, 1989, Trinity University, San Antonio, Texas and by F.M. at the 4th Annual Conference on Undergraduate Research, April 21, 1990, Union College, Schenectady, New York.

(2) Nicholas was the first to demonstrate the intermolecular Friedel-Crafts alkylation involving simple dicobalt hexacarbonyl-stabilized propargyl cations: Lockwood, K. F.; Nicholas, K. M. *Tetrahedron Lett.* **1977**, *18*, 4163. For a review of the use of cobalt-stabilized carbocations see: Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207.

(3) Schreiber, S. L.; Klimas, M. T.; Sammakia, T. *J. Am. Chem. Soc.* **1987**, *109*, 5749.

(4) Barrow, C. J., Bright, S. T.; Coxon, J. M.; Steel, P. J. *J. Org. Chem.* **1989**, *54*, 2542.

(5) Belanger, P. C.; Dufresne, C.; Scheigetz, J.; Young, R. N.; Springer, J. P.; Dmitrienko, G. I. *Can. J. Chem.* **1982**, *60*, 1019.

(6) All new compounds, with the exception of **7a,b,c** and **13**, gave 300 or 500 MHz ^{1}H NMR, IR, and mass spectra that were in accord with their assigned structure. Infrared spectra only were obtained for **7a,b,c** and **13**.

(7) Seyferth, D.; Wehman, A. *J. Am. Chem. Soc.* **1970**, *92*, 5520.

(8) Nicholas, K. M.; Pettit, R. *Tetrahedron Lett.* **1971**, *12*, 3475.

(9) Rhoads, S. J.; Waali, E. E. *J. Org. Chem.* **1970**, *35*, 3358.

(10) We are currently studying this reaction in detail.

(11) Corey, E. J.; Suggs, J. W. Tetrahedron Lett. **1975**, *16*, 2647.

(12) Yamamoto, Y. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 947.

(13) This conversion was carried out by catalytic hydrogenation.

Acknowledgments.

This work was supported by a grant from Research Corporation and by funds generously provided by Eckerd College. We are indebted to Professor Robert A. Holton (Florida State University) for his encouragement and for obtaining 300 and 500 MHz ^{1}H NMR spectra and mass spectra. We would also like to thank Dr. Andrew S. Zektzer (University of South Florida, Tampa) for obtaining high-field ^{1}H NMR spectra and Professor Michael E. Jung (UCLA) for helpful discussion.

(Received in USA 20 July 1990)