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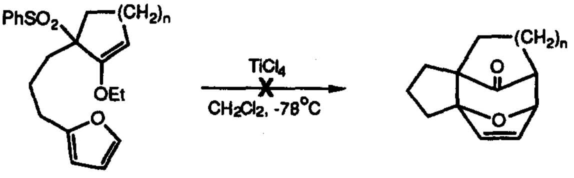
AN INTRAMOLECULAR 4+3 CYCLOADDITION-VINYLOGOUS GROB FRAGMENTATION ROUTE TO A TRICYCLO[6.3.0.$0^{2,4}$]UNDECENE RING SYSTEM

Michael Harmata* and Saleh Elahmad

Department of Chemistry, University of Missouri-Columbia, Columbia MO 65211

Summary: Solvolysis of chloroketone **6** in 3M $LiClO_4$ in ether in the presence of base gave cycloadduct **2a** stereoselectively and in good yield. This cycloadduct could be further transformed via a vinylogous Grob fragmentation to the tricyclo[6.3.0.$0^{2,4}$] undecene ring system **10** in good yield.

As part of a program involving the study of intramolecular 4+3 cycloadditions of allylic cations, we have begun an investigation of the cycloaddition reactions of cyclic alkoxyallylic cations with dienes.[1] Attempts to use methodology we had developed previously to effect the cyclization of **1a** or **1b** failed to yield any cycloadduct.[1a] Thus, treatment of **1a** or **1b** with $TiCl_4$ in CH_2Cl_2 at -78°C resulted in the formation of very small amounts of a carbonyl-containing compound which , while unidentified, was clearly not cycloadduct **2a** or **2b** (Equation 1). Reasoning that the cycloadducts were probably unstable to the reaction conditions, we decided to use milder methods to generate the requisite allylic cations.

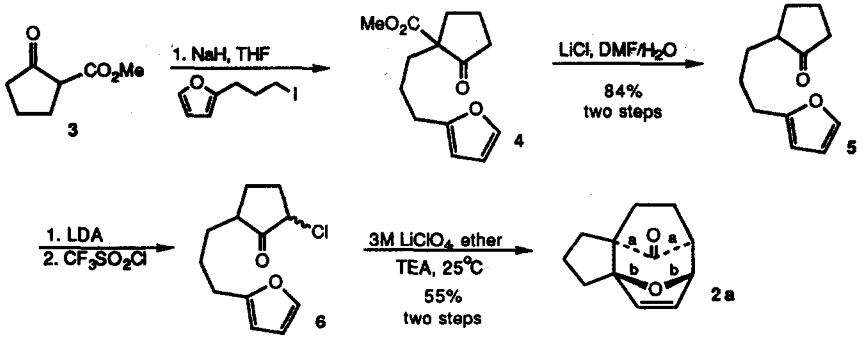


1a: n=1
1b: n=3

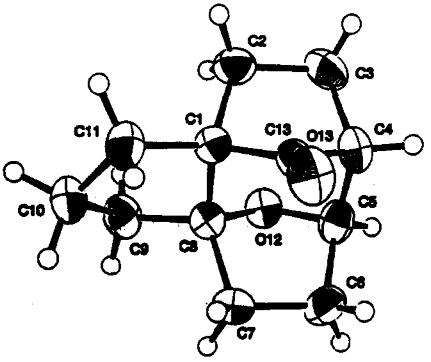
2a: n=1
2b: n=3

Equation 1

The methodology introduced by Föhlisch appeared ideal to solve our problems.[2] An appropriate substrate to test intramolecular cycloaddition was synthesized as shown in Scheme 1. Treatment of methyl 2-cyclopentanone carboxylate with sodium hydride and alkylation of the resultant stabilized enolate with 2-(3-iodopropyl)furan gave ketoester 4 in 91% yield. A Krapcho decarboalkoxylation gave ketone 5 in 79-84% yield.[3] Treatment of 5 with LDA followed by triflyl chloride[4] gave the chloroketone 6.This was dissolved without purification as a .1M solution in 3 M $LiClO_4$ in ether in the presence of excess triethylamine. Cycloadduct 2a was isolated in 55% yield for two steps as a 16:1 mixture of stereoisomers. The stereochemical assignment was made on the basis of X-ray analysis of dihydro-2a. An ORTEP plot is shown in Figure 1.[5,6]



Scheme 1



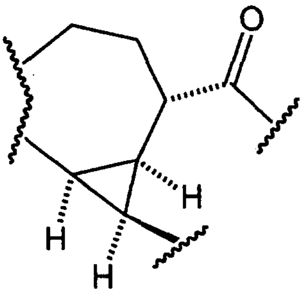
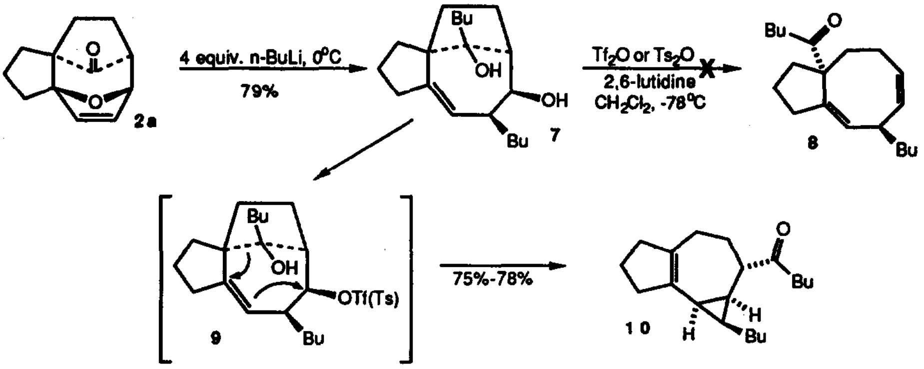


Figure 1 Figure 2

It should be noted that 2a is a fused 5,8 ring system. Formation of an open eight membered ring requires the cleavage of one each of the sets of bonds labelled a and b in 2a. In view of the large number of interesting natural products containing a fused 5,8 ring system,[7] we undertook a study aimed at the conversion of 2a to such a carbocycle.

To that end, 2a was treated with excess n-BuLi according to a procedure introduced by Lautens and co-workers.[8] This gave compound 7 in 77% isolated yield.[9] We conjectured that activation of the secondary hydroxyl group and treatment with base would effect a Grob fragmentation leading to 8.[10] Accordingly, treatment of 7 with either triflic or tosic anhydride in dichloromethane in the presence of 2,6-lutidine was expected to give the corresponding triflate or tosylate derivative. This was not the case. Instead, a rearrangement best described as a vinylogous Grob fragmentation took place to give **10** as a single isomer in very good yield.[11] Presumably alkene assisted departure of the leaving group and carbon-carbon bond fragmentation occurred in a stepwise or concerted fashion to lead to **10**. Alkene participation of this type is well known.[12]

The structure of **10** was established on the basis of spectral data. IR showed a band at 1713 cm^{-1}, indicative of a ketone. Low resolution mass spectrometry gave a parent ion at 288 m/e. The ^{13}C and DEPT spectra showed a total of 20 carbons: 2 methyls, 11 methylenes, 4 methines and 3 quaternary carbons. In particular, quaternary carbons at 213, 135 and 132 ppm suggest the presence of a ketone and a tetrasubstituted alkene. The 1 bond C-H coupling constant for methines at 48, 22 and 17 ppm were around 170 Hz, suggesting the presence of a cyclopropane ring. Finally, a COSY spectrum revealed a connectivity establishing the presence the presence of the fragment shown in Figure 2. NOESY studies were not helpful in confirming stereochemical relationships and these assignments are based on mechanistic considerations.[8]



Scheme 2

Attempts to derivatize **7** as a benzoate ester were successful, but treatment with base resulted only in the formation of elimination products. Removal of the double bond in **7** by hydrogenation and fragmentation attempts have thus far led only to elimination or rearrangement products.

In summary, we have found that a cyclic oxyallylic cation undergoes smooth intramolecular 4+3 cycloaddition stereoselectively and in good yield. The adduct can be transformed to a tricyclo[6.3.0.$0^{2,4}$]undecene system via a vinylogous Grob fragmentation. Further studies of the intramolecular 4+3 cycloaddition of cyclic allylic cations and the chemistry of the cycloadducts are in progress and will be reported in due course.[13,14]

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References and Notes

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(2) (a) Föhlisch, B.; Gehrlach, E.; Herter, R. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 137. (b) Föhlisch, B.; Herter, R. *Chem. Ber.* **1984**, *117*, 2580. (c) Kaiser, R.; Föhlisch, B. *Helv. Chim. Acta* **1990**, *73*, 1504.

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(5) MW=192.26; Space Group: P 21/n; a = 15.1850(20)Å, b = 7.5735(6)Å, c = 8.8187(12)Å, β = 106.024(6)^o; V = 974.78(20)Å^3; Z = 4; Dcalc = 1.310; Radiation = CuKα (1 = 1.5418)Å; μ = 0.00mm^{-1}; F(000) = 416; Temperature = 23=/-1o; Final R = 0.045 for 1391 reflections with I>2σ(I).

(6) Data on **2a**: mp 81-83^{o}C. ^{1}H NMR (CDCl$_3$, 500 MHz) 6.28 (br d, 1H, J=5.7), 6.09 (d, 1H, J=5.8), 4.69 (dd, 1H, J=1.5, 3.4), 2.41 (dd, 1H, J=4, 5.6), 2.17-2.12 (m, 1H), 2.08-1.99 (m, 3H), 1.94-1.69 (m, 4H), 1.5-1.41 (m, 2H); ^{13}C NMR (CDCl$_3$, 125 MHz) 210.42, 135.05, 133.42, 97.10, 83.95, 64.21, 50.26, 29.40, 28.21, 23.22, 21.03, 20.31; IR (KBr) 3074w, 3069w, 2964s, 2948m, 2910w(sh), 2868m, 1743s, 1448m, 1345m, 1128m, 1099m, 1054m, 1004m, 989m, 981s, 951w, 858m, 773m, 713m; MS (70 eV) 190(M$^+$, 69), 162(61), 135(50), 134(62), 133(39), 121(24), 120(11), 119(21), 118(11), 107(20), 106(12), 105(23), 96(33), 95(39), 94(39), 91(54), 82(11), 81(100), 79(33), 78(18), 77(27), 67(19), 66(27), 65(25), 55(68), 53(42), 52(13), 51(21). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.63; H, 7.42. Found: C, 75.57; H, 7.31.

(7) Petasis, N.A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757.

(8) Lautens, M.; Abd-El-Aziz, A.S.; Lough, A. *J. Org. Chem.* **1990**, *55*, 5305.

(9) Data on **7**: ^{1}H NMR (CDCl$_3$, 500 MHz) 5.48 (d, 1H, J=7.8), 4.15 (dd, 1H, J=1.9,6.4), 2.47-2.38 (m, 3H), 2.28-2.23 (m, 1H), 2.08 (ddt, 1H, J=2.6, 5.1, 11.6), 1.98-1.85 (m, 4H), 1.68-1.56 (m, 4H), 1.51-1.14 (m, 13H), 0.94 (t, 3H, J=7.2), 0.91 (t, 3H, J=7.3); ^{13}C NMR (CDCl$_3$, 125 MHz) 149.14, 122.46, 82.32, 68.47, 58.19, 51.36, 44.60, 38.09, 37.46, 32.26, 34.84, 32.02, 30.21, 26.00, 24.19, 23.52, 23.12, 20.38, 14.20, 14.12; IR (KBr) 3499s(br), 3448s(br), 2959s, 2868s, 1468m, 1453w, 1377m, 1352m, 1321m, 1272w, 1248w, 1232m, 1201w, 1162m, 1124w, 1093m, 1069m, 1035s, 992w, 869w, 727w, 708m, 686m. Anal. Calcd for $C_{20}H_{34}O2$: C, 78.38; H, 11.18. Found: C, 78.61; H, 10.97.

(10) Deslongschamps,P. *Stereoelctronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983; pp 257-66.

(11) Data on **10**: ^{1}H NMR (CDCl$_3$, 500 MHz) 2.55-2.44 (m, 2H), 2.36-2.19 (m, 6H), 2.05 (br t, 1H), 1.90-1.70 (m, 5H), 1.60-1.53 (m, 2H), 1.43-1.27 (m, 8H), 1.24-1.20 (m, 2H), 0.94-0.88 (m, 6H); ^{13}C NMR (CDCl$_3$, 125 MHz) 213.33s, 135.62s, 132.43s, 48.12d, 40.70t, 39.46t, 39.11t, 32.18t, 32.15t, 27.51t, 26.01t, 24.26t, 22.99t, 22.76t, 22.48t, 22.32t, 20.42d, 17.56d, 14.13q, 13.93q; IR (neat) 2956s, 2929s, 2866s, 1713s, 1461m, 1408m, 1378m, 1305w, 1240w, 1210w, 1124w, 1044w, 988w, 739m; MS (70 eV) 288(M$^+$, 43) 245(74), 232(56), 231(43), 204(20), 203(100), 189(42), 147(22), 133(46), 131(23), 119(60), 105(28), 91(74), 86(27), 79(28), 67(20), 57(67), 55(29). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27: H, 11.18. Found: C, 83.39; H, 11.12.

(12) For examples and leading references, see: (a) Winstein, S.; Adams, R. *J. Am. Chem. Soc.* **1948**, *70*, 838. (b) Poulter, C.D.; Winstein, S. *J. Am. Chem. Soc.* **1970**, *92*, 4282. (c) Lambert, J.B.; Featherman, S.I. *Tetrahedron Lett.* **1975**, 2663. (d) Lambert, J.B.; Featherman, S.I. *J. Am. Chem. Soc.* **1977**, *99*, 1542.

(13) All new compounds exhibited acceptable ^{1}H and ^{13}C NMR and IR spectral data as well as satisfactory combustion analysis or exact mass data.

(14) Presented in part at the 204th National Meeting of the American Chemical Society, Washington, DC, August 23-28, 1992 ORGN 391.

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