

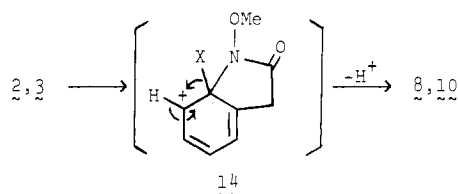
**Table I.** Electrophilic Aromatic Substitution by *N*-Chloro-*N*-methoxyamides

entry <sup>a</sup>	starting compd	product	yield, %
1	<b>1</b>	<b>6</b>	87.5
2	<b>4</b>	<b>11</b>	87
3	<b>5</b>	<b>12</b>	60
4 <sup>b</sup>			68
5 <sup>b</sup>			69
6	PhCON(Cl)OMe + benzene <sup>c</sup>	PhN(OMe)COPh	70.8
7	Me(CH <sub>2</sub> ) <sub>6</sub> CON(Cl)OMe + benzene <sup>c</sup>	PhN(OMe)CO(CH <sub>2</sub> ) <sub>6</sub> Me	93
8 <sup>b</sup>	<b>13</b> + naphthalene <sup>d</sup>		80.1
			10.9

<sup>a</sup>All the experiments were performed by using Ag<sub>2</sub>CO<sub>3</sub> and TFA.

<sup>b</sup>TFA-MeNO<sub>2</sub> (1:1, v/v) was used as solvent. All products were hydrogenated to the corresponding amides, which were identified by the comparison of their melting points with the literature values. <sup>c</sup>10 mol equiv. <sup>d</sup>5 mol equiv.

## Scheme I



available and relatively stable.<sup>4</sup> (2) The experimental conditions are very simple; under the best conditions, the reaction is carried out at ambient temperature with a short reaction time in the presence of the transition-metal salts (Ag<sup>+</sup>, Zn<sup>2+</sup>, Pd<sup>2+</sup>, Fe<sup>2+</sup>, etc.). The electrophilic aromatic chlorination mainly occurred in the absence of metal salts. Addition of 2 equiv of the metal salt to a substrate are usually used to prevent the side reaction. Species of the counteranions of the metal salts are not strictly limited, and in the case of silver salt, anions (CO<sub>3</sub><sup>2-</sup>, SO<sub>4</sub><sup>2-</sup>, BF<sub>4</sub><sup>-</sup>, OAc<sup>-</sup>, OCOCF<sub>3</sub><sup>-</sup>, and OSO<sub>2</sub>CF<sub>3</sub><sup>-</sup>) are effective. Acidic media are essential to the reaction and TFA, formic acid, and acetic acid are used as reaction media, in which TFA usually gives best results. Displacement of protic acids with Lewis acids does not bring good results. (3) Intramolecular as well as intermolecular reactions work well, and the yields based on *N*-chloro-*N*-methoxyamides are high.

In the case of 2-chloro and 2-bromo compounds **2** and **3**, the main products were **7** (71%) and **9** (51%); however, an unexpected mode of cyclization occurred to some extent to give 7-halogeno-1-methoxy-2-oxindoles<sup>5</sup> (**8**, 8.8%, **10**, 12.5%) which could be rationalized by way of an ipso intermediate (**14**) (Scheme I).

Concerning the possible reaction mechanisms, it is assumed that the reactions are initiated by acid-catalyzed heterolysis of the

(4) *N*-Methoxyamides are chlorinated by *tert*-butyl hypochlorite in CH<sub>2</sub>Cl<sub>2</sub> with cooling to give *N*-chloro-*N*-methoxyamides in quantitative yield.

(5) Identification of **8** and **10** was performed by the comparison of the <sup>1</sup>H NMR spectrum with those of other regioisomers (**9** and 5- and 6-bromo-1-methoxy-2-oxindoles).

nitrogen-chlorine bond promoted with metal ions. A nitrenium ion thus generated is stabilized by acid<sup>6</sup> and by the capto-dative (push-pull) effect of the electron-withdrawing carbonyl and electron-donating methoxyl groups, as is stated in the case of the stabilization of aminyl free radicals,<sup>7</sup> and is long-lived enough to react with an aromatic ring. In brief, the carbonyl and the methoxyl groups, acid, and metal ions, all of them, play important roles for the generation and stabilization of a nitrenium ion. This conclusion has been drawn from the following facts: (1) *N*-Chloro-*N*-methyl- and *N*-chloro-*N*-acetoxyphenylacetamides failed to cyclize. (2) Various hydroxy(2-phenylethyl)amines such as *O*-tosyl, *O*-(2-mesitylsulfonyl), *N,O*-diacyl, and *N*-chloro-*O*-acyl compounds failed to cyclize in acidic conditions. (3) Radical mechanisms are not supported because oxygen atmosphere or an addition of a radical scavenger *N,N*-diphenylpicrylhydrazil<sup>8</sup> did not affect the aromatic methoxyamidation reaction at all.

**Registry No.** **1**, 91523-28-3; **2**, 91523-29-4; **3**, 91523-30-7; **4**, 91523-31-8; **5**, 91523-32-9; **6**, 65816-14-0; **7**, 91523-33-0; **8**, 91523-34-1; **9**, 91523-35-2; **10**, 91523-36-3; **11**, 91523-37-4; **12**, 91523-38-5; Ag<sub>2</sub>CO<sub>3</sub>, 534-16-7; Ag<sub>2</sub>SO<sub>4</sub>, 10294-26-5; AgBF<sub>4</sub>, 14104-20-2; AgOAc, 563-63-3; AgOC(O)CF<sub>3</sub>, 2966-50-9; AgOSO<sub>2</sub>CF<sub>3</sub>, 2923-28-6; Zn, 7440-66-6; Pd, 7439-92-1; Fe, 7439-89-6.

(6) Okamoto, T.; Shudo, K.; Ohta, T. *J. Am. Chem. Soc.* **1975**, *97*, 7184.

(7) Viehe, H. G.; Merényi, R.; Stella, L.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 917.

(8) Bastable, J. W.; Hobson, J. D.; Riddell, W. D. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2205.

## A Zinc-Alkyl Caged Cobalt(III) Derivative

Inge I. Creaser, John D. Lydon, and Alan M. Sargeson\*

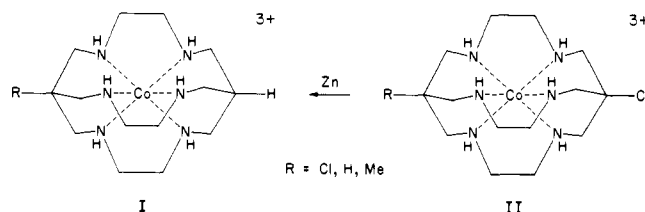
The Research School of Chemistry  
The Australian National University  
Canberra, A.C.T. 2601, Australia

Ernst Horn and Michael R. Snow

Department of Physical and Inorganic Chemistry  
University of Adelaide  
Adelaide, S.A. 5001, Australia

Received April 9, 1984

During the syntheses of the proton-capped cage complexes (I) by reduction of the chloro-capped species (II) with zinc dust in



water,<sup>1</sup> species were isolated which analyzed for CoC<sub>14</sub>H<sub>31</sub>N<sub>6</sub>ZnCl<sub>4</sub>·2H<sub>2</sub>O (from II, R = Cl) and CoC<sub>15</sub>H<sub>33</sub>N<sub>6</sub>ZnCl<sub>4</sub>·2H<sub>2</sub>O (from II, R = Me). The UV-visible spectra were similar to those of I, and the <sup>1</sup>H NMR spectra exhibited a complex group of resonances centered at ca. 3 ppm (ref TPS, TPS = 2,4,6-triisopropylbenzenesulfonate) characteristic of other unsymmetrically capped (hexaaza-bicyclo[6.6.6]icosane)cobalt(III) complexes.<sup>2</sup> The <sup>13</sup>C NMR spectra were also consistent with intact cage complexes, incorporating two resonances at -29.5 and -30.9 ppm (product from II, R = Cl) and -24.8 and -30.4 ppm vs. dioxane

(1) Geue, R. J.; Hambley, T. W.; Harrowfield, J. MacB.; Sargeson, A. M.; Snow, M. R. Submitted for publication in *J. Am. Chem. Soc.*

(2) Lay, P. A. Doctoral Dissertation, The Australian National University, 1981.

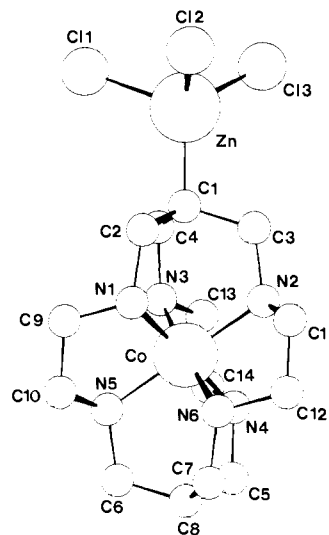
(product from II, R = Me). Two of these chemical shifts coincide with those of bridgehead carbons in a wide range of H- and H<sub>3</sub>C-capped cage complexes of the type dealt with here, i.e.,  $-30.4 \pm 0.9$  (H) and  $-24.4 \pm 0.5$  ppm (H<sub>3</sub>C).<sup>2</sup> This correlation leads to the assignment of the new resonances to bridgehead carbons opposite the H and Me ends of the new species.

Cyclic voltammetry in 0.1 M NaClO<sub>4</sub> at a hanging mercury drop electrode (HMDE) gave quasi-reversible waves at  $-0.88$  (product from II, R = Cl) and  $-0.86$  V (product from II, R = Me) vs. SCE, with peak separations of 75 and 100 mV, respectively, at 100 mV/s scan rate. The fully reduced species I exhibits Co(III)/(II) couples at  $-0.67$  (R = H) and  $-0.65$  V (R = Me) under the same conditions.

Cobalt(III)/(II) redox potentials for hexaammine cage complexes are known to be sensitive to the nature of the apical substituent.<sup>2,3</sup> The observed redox potentials for these new complexes indicate an apical functional group with a negative inductive substituent effect relative to H and CH<sub>3</sub>. This, along with the other data, leads us to infer the formation of unusually stable organozinc complexes. This has now been established by a single-crystal X-ray structural analysis of III (R = H) (Figure 1) as the chloride. The crystals of formula C<sub>14</sub>H<sub>35</sub>Cl<sub>4</sub>CoN<sub>6</sub>O<sub>2</sub>Zn are monoclinic, space group P2<sub>1</sub>/c, with  $a = 8.625$  (1) Å,  $b = 16.273$  (5) Å,  $c = 15.381$  (4) Å,  $\beta = 93.12$  (1)°,  $d_{\text{meas}} = 1.68$  g cm<sup>-3</sup>,  $d_{\text{calcd}} = 1.697$  g cm<sup>-3</sup>, and  $Z = 4$ . The 2544 nonzero reflections were collected on a CAD4 diffractometer and solved by Patterson techniques. Full-matrix least-squares refinement with anisotropic thermal parameters for non-hydrogen atoms converged with an  $R_w$  value of 0.032.<sup>5</sup>

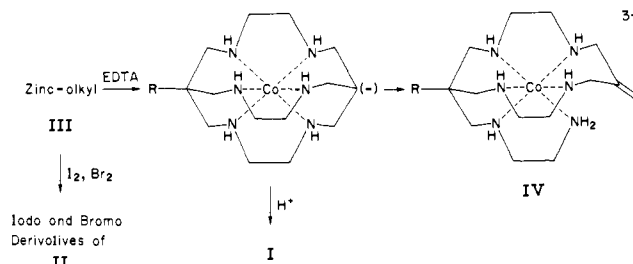
The zinc-carbon bond in these complexes appears extraordinarily stable. The complexes were isolated from 6 M HCl, and hydrolysis of the alkyl-zinc bond in this medium at 75 °C gave observed rate constants of  $9 \times 10^{-5}$  (R = H) and  $1 \times 10^{-4}$  s<sup>-1</sup> (R = Me). Prolonged heating on a steam bath in neutral or basic solutions also liberated Zn(II), and the product of hydrolysis in acid, neutral, or basic conditions was I. This stability contrasts drastically with that of alkylzinc compounds in general. Most react vigorously with oxygen and water.<sup>6</sup> The complexes dealt with here have stabilities akin to those of the very hindered tris(trimethylsilyl)methylzinc compounds which also exhibit substantial thermal and chemical resistance.<sup>7</sup> Both species are much less reactive than the *tert*-butylzinc alkyl compounds which are hindered to a substantial degree and more so than the zinc alkyl cage. We presume therefore that the stability arises more from the electron-withdrawing effect of the Co(III) cage and its positive charge than from hindered attack of the reagent. The Zn-C bond length, 2.049 (4) Å, is within the range of values 1.95–2.07 Å determined for zinc-alkyl species<sup>9-11</sup> and is somewhat longer than the most accurate value 1.963 (5) Å<sup>11</sup> for a zinc ethyl species.

In the presence of Na<sub>2</sub>EDTA the rate of Zn-C cleavage was significantly faster. At 75 °C in 0.1 M Na<sub>2</sub>EDTA the observed



**Figure 1.** Atom numbering scheme for III. Some distances (Å): Zn-Cl(1), 2.374 (1); Zn-Cl(2), 2.300 (2); Zn-Cl(3), 2.291 (1); Zn-C(1), 2.049 (4); Co-N(1), 1.971 (4); Co-N(2), 1.974 (4); Co-N(3), 1.979 (4); Co-N(4), 1.988 (4); Co-N(5), 1.986 (4); Co-N(6), 1.986 (4). Angles: C<sub>3</sub>-C<sub>1</sub>-C<sub>2</sub>, 111.9 (4)°; C<sub>4</sub>-C<sub>1</sub>-C<sub>2</sub>, 110.3 (4)°; C<sub>7</sub>-C<sub>8</sub>-C<sub>5</sub>, 112.4 (5)°; C<sub>6</sub>-C<sub>8</sub>-C<sub>5</sub>, 111.6 (4)°; N<sub>6</sub>-Co-N<sub>2</sub>, 86.2 (2)°; N<sub>4</sub>-Co-N<sub>3</sub>, 85.4 (2)°; N<sub>5</sub>-Co-N<sub>1</sub>, 86.4 (2)°.

rates were  $7 \times 10^{-3}$  (R = H) and  $6 \times 10^{-3}$  s<sup>-1</sup> (R = Me). Two products arose from this treatment: the proton-capped I and a



yellow complex exhibiting two signals in the <sup>1</sup>H NMR spectrum at 5.62 and 5.68 ppm (R = H) and 5.46 and 5.58 ppm (R = Me) vs. TPS and two in the <sup>13</sup>C NMR spectrum at 66.0 and 60.4 ppm vs. dioxane (R = Me), both sets of signals characteristic of an olefin. These data and elemental analyses lead us to formulate IV for these species. Both the alkyl and olefin products are consistent with the formation of a bridgehead carbanion intermediate by loss of Zn(II). The carbanion can then capture a proton from the solvent or rearrange to the olefin with subsequent protonation of the aminato ion. The zincalkyl complexes also react with other electrophilic reagents including the halogens Br<sub>2</sub> and I<sub>2</sub> to produce the halo-substituted cages II.

The insertion of Zn between the C-Cl bond in these complexes can be viewed as oxidative addition, and the reaction implies possible reactivity for other finely divided metals suitably activated, using appropriate C-X (X = Cl, Br, I) cages. The alkyl halides may also react with low-valent phosphine complexes via the oxidative addition mode, and such a reaction could indicate something of the steric requirements for such oxidative additions. Finally, the unusual stability of the zincalkyl cage molecules also implies the possibility of relatively stable Mg and Cd alkyl complexes and maybe of Al, Ti, Cu, Co, and Ni complexes as well.

**Acknowledgment.** We are grateful to the Australian Research Grants Scheme for support.

**Registry No.** I (R = H), 85664-13-7; I (R = Me), 85664-11-5; II (R = Cl), 85663-90-7; II (R = Me), 85663-93-0; III-Cl (R = H), 91550-95-7; III-Cl·2H<sub>2</sub>O (R = H), 91550-96-8; III-Cl (R = Me), 91550-97-9; IV (R = H), 91550-98-0; IV (R = Me), 91550-99-1.

(3) Bond, A. M.; Lawrance, G. A.; Lay, P. A.; Sargeson, A. M. *Inorg. Chem.* **1983**, *22*, 2010–2021.

(4)  $R_w = (\sum(|F_o| - |F_c|)|w|^{1/2}) / (\sum(|F_o|(w)^{1/2})$ ;  $w = 1.37 / (\sigma^2 F_o + 0.00037 F_o^2)$ .

(5) Programs used included SUSDAD data reduction program for the CAD4 diffractometer, University of Sydney, 1976; SHELX, "Program for crystal structure determination"; Sheldrick, G. M.; 1976; and PLUTO-plotting by Motherwell, W. D. S.

(6) "Methods of Elemento-Organic Chemistry"; Sheverdina, N. I., Rocheshkov, R. A., Eds.; North-Holland Publishing Co.: Amsterdam, 1967; Vol. 3, p 72.

(7) Eaborn, C. L.; Retta, N.; Smith, J. D. *J. Organomet. Chem.* **1980**, *190*, 101–106.

(8) "Comprehensive Organometallic Chemistry"; Wilkinson, G., Ed.; Pergamon Press: New York, 1982; Vol. 2, pp 823–862.

(9) Shearer, H. M. M.; Spencer, C. B. *Acta Crystallogr., Sect. B* **1980**, *B36*, 2046–2050.

(10) Ishimori, M.; Hagiwara, T.; Tsuruta, T.; Kai, Y.; Yasuoka, N.; Kasai, N. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1165–1166.

(11) van Santvoort, F. A. J. J.; Krabbendam, H.; Spek, A. L.; Boersma, J. *Inorg. Chem.* **1978**, *17*, 388–394.

**Supplementary Material Available:** Tables of atomic positional and thermal parameters, interatomic distances and angles, and a list of observed and calculated structure factors (17 pages). Ordering information is given on any current masthead page.

## Synthesis of the Taxane Ring System

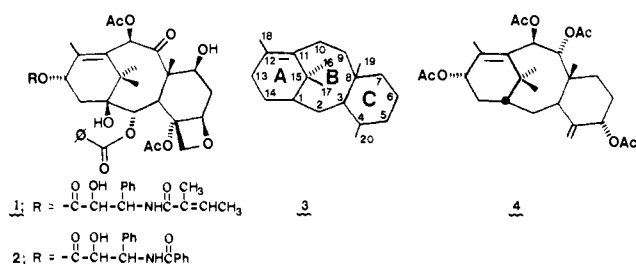
Robert A. Holton

Department of Chemistry  
Virginia Polytechnic Institute and State University  
Blacksburg, Virginia 24061

Received April 23, 1984

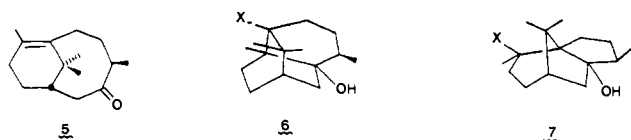
The taxane family of diterpenes<sup>1</sup> has attracted interest in both the biological and chemical communities. Cephalomannine (**1**) and taxol (**2**) have been found to exhibit significant antitumor properties.<sup>2</sup> The structural complexity of these molecules presents a formidable synthetic challenge, and some preliminary synthetic studies have recently been described.<sup>3</sup>

We have embarked upon a taxane synthesis program featuring three sequential objectives: (1) an efficient synthesis of the tricyclic taxane ring system **3**, (2) total synthesis of a modestly function-



alized naturally occurring taxane such as taxusin (**4**), and (3) synthesis of the fully functionalized molecules **1** and **2**. We describe herein the realization of the first of these objectives.

Our initial plan for the synthesis of the taxane ring system involved annulation of ring C onto hydroxy ketone **5** using standard methodology. Preparation of **5** was envisioned to provide a significant challenge. We considered the fragmentation of either **6** or **7** to hold promise for this purpose. The structural similarity



- (1) For a recent review, see: Miller, R. W. *J. Nat. Prod.* **1980**, *43*, 425.  
 (2) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325. Miller, R. W.; Powell, R. G.; Smith, C. R., Jr. *J. Org. Chem.* **1981**, *46*, 1469 and references contained therein.  
 (3) Several approaches to the synthesis of various versions of the taxane ring system have been reported: (a) Intramolecular Diels-Alder approaches: Sakan, K.; Craven, B. M. *J. Am. Chem. Soc.* **1983**, *105*, 3732. Brown, P. A.; Jenkins, P. R.; Fawcett, J.; Russell, D. R. *Chem. Commun.* **1984**, 253. Shea, K. J.; David, P. D. *Agnew. Chem., Int. Ed. Engl.* **1983**, *22*, 419. (b) Anionic oxy-Cope approach: Martin, S. F.; White, J. B.; Wagner, R. *J. Org. Chem.* **1982**, *47*, 3192. (c) Fragmentation approach: Trost, B. M.; Hiemstra, H. *J. Am. Chem. Soc.* **1982**, *104*, 886.

of **6** and patchouli alcohol led us to discover that Buchi's elegant synthesis of the natural product<sup>4</sup> suggested a readily available fragmentation substrate.

Therefore, following the Buchi procedure,  $\beta$ -patchouline oxide (**8**)<sup>5</sup> was converted ( $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ) to the tertiary alcohol **9** in 65% yield.<sup>6</sup> Hydroxyl-directed epoxidation<sup>7</sup> of **9** gave an unstable substance which underwent fragmentation in situ to provide keto alcohol **10**.<sup>8-10</sup> The **9**  $\rightarrow$  **10** conversion was found to proceed quantitatively<sup>6</sup> under the following conditions: first, treatment of a methylene chloride solution of **9** with *t*-BuOOH (1.0 mol equiv) and  $\text{Ti}(\text{O}-i\text{-Pr})_4$ <sup>11</sup> (1.0 mol equiv) at 0 °C for 1 h then addition of dimethyl sulfide (5 mol equiv) followed by warming the solution to reflux for 5-8 h.

Unexpectedly, attachment of ring C proved to be troublesome. Hydroxy ketone **10** was first converted to MOM ether **11**<sup>8</sup> ( $\text{CH}_3\text{OCH}_2\text{Cl}$ ,  $\text{EtN}(i\text{-Pr})_2$ ,  $\text{CH}_2\text{Cl}_2$ , 0 °C, 12 h, 98%).<sup>6</sup> Treatment of **11** with BMDA/TMSCl/ $\text{Et}_3\text{N}$ <sup>12</sup> gave exclusively the desired more-substituted enol ether,<sup>13</sup> which, upon treatment with methylolithium in DME followed by trimethylsilyl methyl vinyl ketone<sup>14</sup> at -78  $\rightarrow$  0 °C, was converted to diketone **12**<sup>8</sup> as a single stereoisomer<sup>13</sup> in 93% yield<sup>6</sup> from **11**.

Aldol condensation of **12** was found to be most difficult. None of the commonly used conditions for the transformation (employing sodium or potassium counterions) gave a cyclized product.

(4) Buchi, G.; MacLeod, W. D., Jr. *J. Am. Chem. Soc.* **1962**, *84*, 3205. Buchi, G.; Erickson, R. E.; Wakabayashi, K. *Ibid.* **1961**, *83*, 927. Dobler, M.; Dunitz, J. D.; Gubler, G.; Weaver, H. P.; Buchi, G.; Padilla, J. *Proc. Chem. Soc.* **1963**, 383. Buchi, G.; MacLeod, W. D., Jr.; Padilla, J. *J. Am. Chem. Soc.* **1964**, *86*, 4438.

(5) Prepared from patchouli alcohol in 95% overall yield via a two-step procedure: (a)  $\text{I}_2$ , benzene; (b) *m*-CPBA,  $\text{CH}_2\text{Cl}_2$ . Alternately, epoxide **8** is available in bulk from International Flavors and Fragrances, Inc., under the trade name Patchino.

(6) All yields refer to isolated, chromatographically and spectrally homogeneous substances.

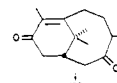
(7) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63 and references contained therein.

(8) Elemental composition of this substance has been verified by combustion analysis within 0.3% of theory or high-resolution mass spectroscopy; some analytical samples were purified by Dr. S. B. Hendi.

(9) Spectral data (taxane numbering): <sup>1</sup>H NMR (250 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  0.92 (3 H, *J* = 5.8 Hz, H-19), 0.93 (3 H, s, H-17), 1.35 (3 H, s, H-16), 1.57 (3 H, s, H-18), 1.68 (1 H, dd,  $J_{\text{gem}} = 11.5$ ,  $J_{\text{ic}} = 5.3$  Hz, H-2), 1.78 (2 H, m, H-9), 1.84 (1 H, dd,  $J_{\text{gem}} = 15$ ,  $J_{13-14} = 3.4$  Hz, H-4 $\alpha$ ), 1.96 (1 H, dddd, H-1), 2.15 (1 H, ddq, H-8), 2.45 (2 H, dd, dd, H-10 $\alpha,\beta$ ), 2.74 (1 H, ddd,  $J_{\text{gem}} = 15$ ,  $J_{14-1} = 7.5$ ,  $J_{13-14} = 10$  Hz, H-14 $\beta$ ), 2.87 (1 H, dd,  $J_{\text{gem}} = 11.5$ ,  $J_{1-2} = 1$  Hz, H-2), 4.14 (1 H, dd, *J* = 10,  $\sim$ 3 Hz, H-13).

(10) Reactions similar to this novel fragmentation have been encountered by Professor S. Dev in the course of his elegant pursuit of longifolene chemistry; see: Dev, S. *Acc. Chem.* **1981**, *14*, 82 and references contained therein. One noteworthy feature of the fragmentation leading to **10** is the syn periplanar orientation of the breaking bonds. In ancillary studies we have found that the syn periplanar relationship between breaking bonds is required for facile fragmentation in a related bridged bicyclic system: Holton, R. A.; Kennedy, R. M. *Tetrahedron Lett.*, in press.

(11) We have found  $\text{Ti}(\text{O}-i\text{-Pr})_4$  to be most effective for this transformation. Use of more acidic catalysts generally led to poorer results due to premature fragmentation of **9**. For example, substitution of  $\text{VO}(\text{AcAc})$  for  $\text{Ti}(\text{O}i\text{Pr})_4$  led to the production of **10** (83% yield)<sup>6</sup> contaminated by diketone **i** (17% yield). Oxidation of **10** to **i** is a very facile process and can be avoided



only under carefully controlled reaction conditions. Oxidation of **10** with Jones reagent affords **i** quantitatively.

(12) Krafft, M. E.; Holton, R. A. *Tetrahedron Lett.* **1983**, *24*, 1345.  
 (13) Hydrolysis of this enol ether led to a 1:1 mixture of **11** and its C8 epimer. These could be separated by careful flash chromatography. Assignment of C8 stereochemistry in **11**, the C8 epimer of **11**, and **12** is based on a <sup>1</sup>H NMR study utilizing europium shift reagent. Upon addition of  $\text{Eu}(\text{fod})_3$  to a  $\text{CDCl}_3$  solution of **11**, downfield shifts of proton resonances were observed consistent with primary complexation of shift reagent with C13 allylic oxygen. Protons attached to C19  $\beta$  methyl were observed to shift upfield slightly. Shifts observed upon addition of  $\text{Eu}(\text{fod})_3$  to a  $\text{CDCl}_3$  solution of the C8 epimer of **11** were again consistent with primary complexation as the C13 oxygen. However, in this case, a significant downfield shift of C19 methyl resonance was observed. A similar study involving **12** again showed  $\text{Eu}(\text{fod})_3$  complexation at C13 oxygen, and in this case the C19 methyl resonance shifted slightly upfield. This result supports structure **12** and is inconsistent with an epimeric formulation at C8.

(14) Stork, G.; Ganem, G. *J. Am. Chem. Soc.* **1947**, *69*, 6181.