Chromium(0) Carbene Complexes Bearing Imino Tethers: Synthesis and Photochemical Reactivity

Benito Alcaide,*[1a] Luis Casarrubios,[1a] Gema Domínguez,[1a,2] Miguel A. Sierra,*[1a] and Angeles Monge[1b,3]

Departamento de Química Orgánica I and Laboratorio de Difracción de Rayos-X
Facultad de Química, Universidad Complutense
28040 Madrid, Spain

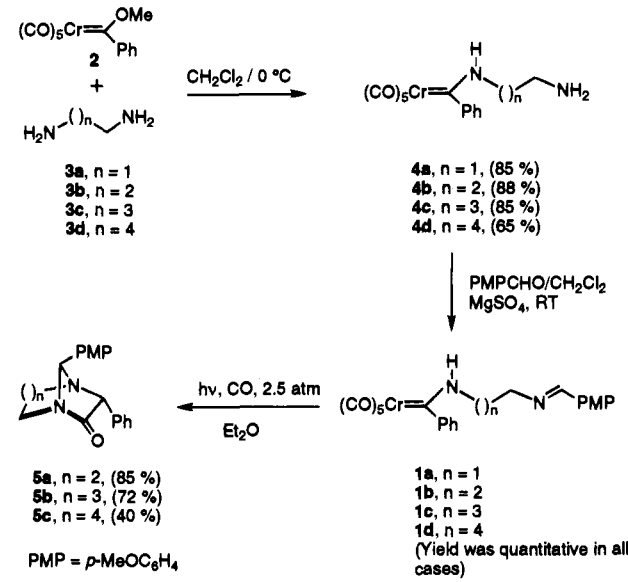
Received February 16, 1995

The ability of chromium(0) carbene complexes to behave as ketene-like reagents under photochemical conditions was reported by McGuire and Hegedus more than 10 years ago.[4] Since then, the photochemistry of these complexes has resulted in an impressive number of different applications in organic synthesis.[5] The intramolecular photochemical reactivity of complexes with ketene acceptors tethered to the carbene carbon has been simultaneously developed. Thus, bicyclic cyclobutanones,[6] lactones,[7] aromatic systems,[8] 1,4-oxazin-2-ones,[9] and butyrolactones[10] are easily available from complexes having C−C double bonds, carbonyl groups, aromatic rings, and hydroxyl functional groups appropriately attached to their structures, respectively. However, the intramolecular version of the original chromium(0) carbene−imine photocycloaddition has not been studied yet. Reported here are the synthesis and preliminary studies of the photochemical reactivity of chromium(0) carbene complexes **1** having an imino tether in their structure.

Condensation of alkoxy phenyl chromium(0) carbene **2** with diamines **3a−d** gave the corresponding diamino carbenes **4a−d** almost instantaneously in nearly quantitative yields.[11] Complexes **4a−d** were transformed into the imino complexes **1a−d** by stirring a solution of carbene and the corresponding aldehyde in the presence of $MgSO_4$ (Scheme 1). Complexes **1** were obtained as spectroscopically pure compounds stable for weeks at −20 °C but decomposing within days at room temperature, or upon flash chromatography regardless of the adsorbent and conditions used.

Except for complex **1a,** which was unreactive, the irradiation (Pyrex, 450-W Hg lamp) of complexes **1b−d** followed by oxidation of the crude reaction mixtures to eliminate the metallic moiety resulted in the exclusive formation of a single diastereoisomer of the products which incorporate a CO functional group in their structures. Products **5a−c** were obtained as analytically pure compounds by recrystallization of the crude

Scheme 1



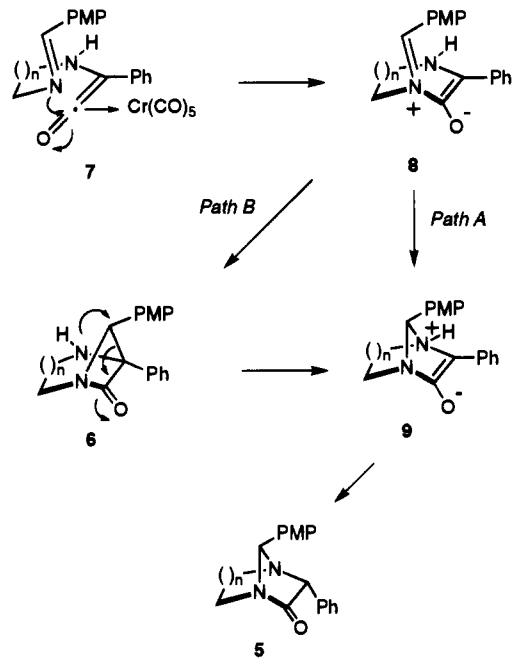
reaction mixtures.[12] The spectroscopic data for these compounds were slightly different from those of the expected bridged β-lactams **6** (Scheme 2). An anomalous low-field resonance of the CO group in their ^{13}C NMR spectra (ca. 194.7−176.0 ppm), the appearance of two singlets at ca. 4.5−5.3 ppm in their ^1H NMR spectra, and the absence of NH absorption in the IR spectra pointed to a different reaction product, even assuming that the high degree of pyramidalization expected for the β-lactam nitrogen would be responsible for these effects. It soon became evident that a structure of bridged γ-lactam **5** was more congruent with the spectroscopic data. Adequate crystals of the cyclization product of complex **1b** were grown and submitted for an X-ray diffraction analysis, confirming the structure of γ-lactam **5** for these compounds. Compounds **5** are members of the family of compounds called "anti-Bredt" amides,[13] which share the common feature of a highly pyramidalized lactam nitrogen. Two spectroscopic effects related with the degree of pyramidalization of the amide nitrogen are observed: in the ^{13}C NMR CO amide signal, which moves upfield with the size of the ring (194.7 ppm for the [3.2.1]-bicyclic system to 175.5 ppm for the [5.2.1] system), and in

(1) (a) Dpto. de Química Orgánica. (b) Laboratorio de Difracción de Rayos-X.
(2) Present address: Unidad de Química Orgánica, Universidad de San Pablo-CEU. Madrid-Spain.
(3) To whom inquires regarding X-ray structural determination should be addressed.
(4) McGuire, M. A.; Hegedus, L. S. *J. Am. Chem. Soc.* **1982**, *104*, 5538. Hegedus, L. S.; McGuire, M. A.; Schultze, L. M.; Chen, Y.; Anderson, O. P. *J. Am. Chem. Soc.* **1984**, *106*, 2680.
(5) Miller, M.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 6779. Pulley, S. R.; Hegedus, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 9037 and references therein.
(6) Söderberg; B. C.; Hegedus, L. S.; Sierra, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 4364.
(7) Colson, P.-J.; Hegedus, L. S. *J. Org. Chem.* **1994**, *59*, 4972.
(8) Merlic, C. A.; Xu, D.; Gladstone, B. G. *J. Org. Chem.* **1993**, *58*, 538.
(9) Vernier, J.-M.; Hegedus, L. S.; Miller, D. B. *J. Org. Chem.* **1992**, *57*, 6914.
(10) Schmeck, C.; Hegedus, L. S. *J. Am. Chem. Soc.* **1994**, *116*, 9927.
(11) Complexes **4** are obtained in the reaction conditions described in ref 12. Other molar ratios of reagents (complex **2**/diamine **3**, 2:1, slow addition of the amine in CH_2Cl_2 solution at room temperature) resulted in formation of bis-aminocarbenes in good yields. The synthesis and reactivity of these complexes will be reported in due time.

(12) The three-step synthesis of compound **5a** from alkoxy chromium carbene **2** is representative (a) Pentacarbonyl[[[(3-aminopropyl)amino]-(phenyl)carbene]chromium(0), **4b**: 1.42 g (19.2 mmol) of net 1,3-diaminopropane was added in one portion via syringe to a cooled (0 °C, ice bath) solution of pentacarbonyl[(methoxy)(phenyl)carbene]chromium-(0) (3.0 g, 9.6 mmol) in anhydrous CH_2Cl_2 (60 mL) under argon. The resulting solution was stirred for 10 min at 0 °C. The solvent was removed in vacuo. After chromatography 3.0 g (88%) of **4b** was obtained as a bright yellow crystalline solid: mp 82−84 °C. (b) Pentacarbonyl[[[3-(*p*-anisylideneamino)propyl]amino](phenyl)carbene]chromium (0), **1b**. A solution of 2.0 g (5.7 mmol) of the aminocarbene **4b** and *p*-anisaldehyde (0.55 g, 4.0 mmol) was stirred for 24 h at room temperature in anhydrous Et_2O (50 mL) in the presence of anhydrous $MgSO_4$ (50 g) under argon. The mixture was then filtered through a sintered glass funnel. The solvent was eliminated in vacuo, and the iminocarbene (pure by ^1H NMR) was obtained as a yellow oil and used without further purification due to its instability: yield 1.9 g (100%). (c) 8-(*p*-Anisyl)-7-phenyl-1,5-diazabicyclo[3.2.1]octan-6-one, **5a**. A solution of iminocarbene complex **1b** (0.97 g, 2.1 mmol) in degassed dry Et_2O (50 mL) was saturated with CO, pressurized to 2.5 atm of CO, and irradiated for 24 h in a Pyrex test tube. The resulting reaction mixture was filtered, and the solvent was removed in vacuo. The dark brown residue was dissolved in EtOAc, filtered through a short pad of Celite, diluted with 1 volume of hexanes, and air oxidized under direct sunlight. The resulting colorless solution with a black precipitate was filtered and the solvent removed in vacuo. The crude amide was purified by recrystallization from $CHCl_3$/pentanes mixtures to give 0.53 g (85%) of analytically pure amide **5a**: mp 128−130 °C. Full experimental procedures and spectroscopic data for the synthesis of compounds **1**, **4**, and **5** are included in the supplementary material.
(13) Hall, H. K.; El-Shekeil, A. *Chem. Rev.* **1983**, *83*, 549.

0002-7863/95/1517-5604$09.00/0

Scheme 2



the analogous displacement to lower frequencies in the ν CO in their IR spectra (from 1765 cm^{-1} for the [3.2.1]bicyclic system to 1715 cm^{-1} for the [5.2.1] system).[14] Among other interesting properties, compounds related to **5** show a striking behavior toward hydrolysis[14c,e] and have been used as models for the acylation step of serine proteases.[14d]

The reaction pathway which ultimately leads to bicycles **5** may start with the generation of ketene intermediate **7**,[15] which would evolve to zwitterion **8** similar to the currently accepted mechanism for the Staüdinger reaction.[16] This zwitterion may evolve to the final products **5** by attack of the amine nitrogen on the iminium ion to give the intermediate **9** followed by proton interchange (path A, Scheme 2). Alternatively, the classical conrotatory ring closure of zwitterion **8**, the accepted second step in the reaction between ketene precursors and imines,[16] would yield β-lactams **6**.[17] Due to their instability, compounds **6** would yield the final products by attack of the amine nitrogen at the C4 carbon of the 2-azetidinone ring to give the intermediate **9** followed by reprotonation of the enolate (path B, Scheme 2).[18] Making a distinction between both reaction pathways must await further experimental data.

In conclusion, a novel, high-yielding entry to bicyclic "anti-Bredt" γ-lactams by the intramolecular photochemical reaction of novel complexes **1** having imino tethers is reported. Further applications of this reaction and the development of complexes structurally related to **1** are underway in our laboratories.

Acknowledgment. Support for this work under Grants PB93-0442 (DGICYT-MEC, Spain) and 290/2 from the CAM (Madrid, Spain) is gratefully acknowledged.

Supplementary Material Available: Full experimental procedure for the preparation of products **1**, **4**, and **5** including compound characterization data, X-ray data for compound **5a**, and ^{1}H- and ^{13}C-NMR spectra of compounds **1**, **4**, and **5** (16 pages); observed and calculated structure factors for $C_{19}O_2N_2H_{20}$ (27 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA950537Q

(14) These effects are a preliminary indication of the extent to which the NC=O resonance is inhibited, which is the cause of the bizarre properties of these and related systems. For selected examples, see: Brouillette, W. J.; Einspahr, H. M. *J. Org. Chem.* **1984**, *49*, 5113. Collins, T. J.; Coots, R. J.; Furutani, T. T.; Keech; J. T.; Peake, G. T.; Santarsiero, B. D. *J. Am. Chem. Soc.* **1986**, *108*, 5333. Somayaji, V.; Brown, R. S. *J. Am. Chem. Soc.* **1987**, *109*, 4738. Somayaji, V.; Skorey, K. I.; Brown, R. S. *J. Org. Chem.* **1986**, *51*, 4866. Slebocka-Tilk, H.; Brown, R. S. *J. Org. Chem.* **1987**, *52*, 805.

(15) Hegedus, L. S., de Weck, G.; D'Andrea S. *J. Am. Chem. Soc.* **1988**, *110*, 2122.

(16) Recent references in both the experimental and the theoretical approaches to the mechanism of the Staüdinger reaction: Hegedus, L. S.; Montgomery, J.; Narukawa, Y.; Snustad, D. C. *J. Am. Chem. Soc.* **1991**, *113*, 5784. Dumas, S.; Hegedus, L. S. *J. Org. Chem.* **1994**, *59*, 4967. Cossio, F. P.; Arrieta, A.; Lecea, B.; Ugalde, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 2085. López, R.; Sordo, T. L.; Sordo, J. A.; González, J. *J. Org. Chem.* **1993**, *58*, 7036.

(17) A multistep synthesis of 1,3-bridged β-lactams analogous to **6** through the Rh-catalyzed insertion of a diazo ketone into the lactam NH bond has been reported by Williams. Williams, R. M.; Lee, B. H.; Miller, M. M.; Anderson, O. P. *J. Am. Chem. Soc.* **1989**, *111*, 1073.

(18) This type of fragmentation is well documented for 2-azetidinones having amino groups attached to the C4 carbon of the four-membered ring. Bose, A. K.; Kugajevsky, I. *Tetrahedron* **1967**, *23*, 957. It is also closely related to the mechanism of fragmentation of 1-azapenams and related systems. Hegedus, L. S.; Moser, W. H. *J. Org. Chem.* **1994**, *59*, 7779.