7398 *J. Am. Chem. Soc.* **2000,** *122,* 7398−7399

Acylamino Chromium Carbene Complexes: Direct Carbonyl Insertion, Formation of Münchnones, and Trapping with Dipolarophiles

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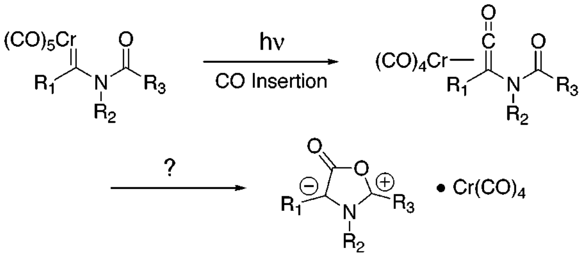
Received September 27, 1999

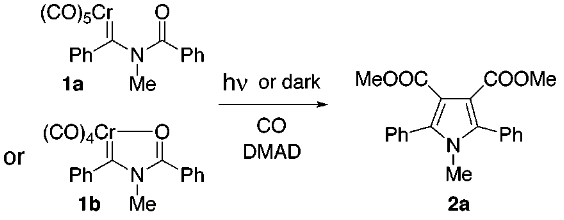
Photolysis of chromium Fischer carbene complexes has become an established synthetic method for the synthesis of a wide range of products including *β*-lactams, amino acids, peptides, cyclobutanones, and arenes, principally due to the extensive studies by Hegedus and co-workers.[1,2] The presumed photogenerated intermediate is a chromium-complexed ketene resulting from insertion of carbon monoxide.[3] Acylamino chromium carbene complexes in particular have been utilized as substrates for the photochemical synthesis of products such as *β*-amino esters, *β*-lactams, and 2-aminophenols, but can demonstrate markedly different behavior from their nonacylated analogues.[4] More broadly, aminocarbene complexes have been the subject of intense study.[5] We report herein evidence for the direct, nonphotochemical insertion of carbon monoxide at ambient temperature and subsequent formation of Münchnones as reactive intermediates in reactions of acylamino chromium carbene complexes and demonstrate applications to the synthesis of heterocyclic compounds.

Consideration of the ketene intermediate resulting from photolysis of an acylamino chromium carbene complex immediately suggests the possibility of cyclization to a Münchnone or Münchnone complex (eq 1). Münchnones, and related mesoionic compounds, play an important role in heterocyclic synthesis due to their participation in dipolar cycloaddition reactions.[6] Usually generated by the dehydration of acylated amino acids, they have not been formed via an organometallic route to date. Münchnones react with alkynes to form bicyclic intermediates that undergo a cycloreversion reaction losing carbon dioxide and forming pyrroles. Thus, if Münchnones or Münchnone complexes could be formed from acylamino carbene complexes, then a new class of carbene complex plus alkyne annulation reactions leading to pyrroles would be possible.[7]



(1)

As the initial test of the concept, complex **1a**[8] was photolyzed under typical conditions in the presence of dimethyl acetylenedicarboxylate (DMAD).[9] Gratifyingly, pyrrole **2a** was indeed formed as planned, but in only 41% yield. Use of the more stable chelate complex **1b**[10] gave an improved 71% yield of the pyrrole. Unfortunately, variations in the photolytic reaction conditions or changes in the alkyne trap resulted in significantly diminished yields. Knowing that carbene complexes react with alkynes,[11] a control reaction was performed by mixing carbene **1a** and DMAD in THF solvent, pressurizing with 30 psi carbon monoxide, and letting it stand at room temperature *in the dark.* Remarkably, the pyrrole **2a** was formed in 78% yield!



(2)

Carbene **1b** also gave the pyrrole in high yield (90%) under the same conditions of CO pressure in the dark. Reaction of either **1a** or **1b** using an initial CO purge of the solution, but no applied CO pressure, produced pyrrole, but in lower yields. Confirmation of the Münchnone intermediate, as opposed to a reaction pathway involving initial alkyne insertion,[7h,m] was accomplished by pressurizing a THF solution of **1b** in the absence of alkyne. The dark brown solution changed to light yellow within 24 h and the Münchnone, 3-methyl-2,4-diphenyl-1,3-oxazolium-5-oxide, could be isolated by recrystallization from acetonitrile in 27% yield.

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(9) A Pyrex pressure tube containing a solution of carbene complex and 2 equiv of alkyne in THF solvent was pressurized to 40 psi with CO. Photolysis was performed using a 450 W Hanovia medium-pressure mercury lamp and water cooling until the deep orange color of the carbene complex disappeared (2.5 h).

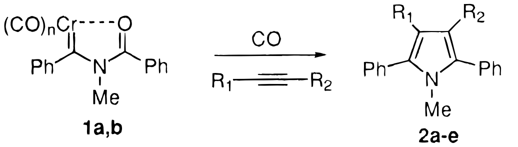
(10) Complex **1a** is an unstable red oil, but complex **1b** forms stable olive-green needles. See Supporting Information.

(11) For a recent review, see: Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271−288.

10.1021/ja9934753 CCC: $19.00

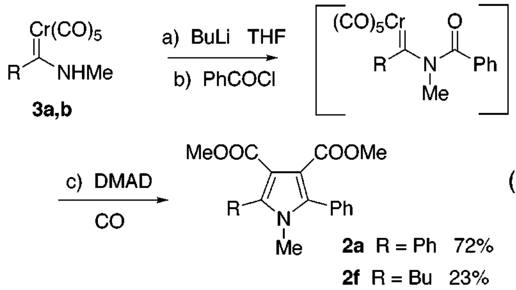
The isolated Münchnone spectroscopically matched an authentic sample prepared independently.[12] Thus, the presumed initial metal-complexed ketene led to a metal-free Münchnone. In the presence of alkyne trap, chromium hexacarbonyl and carbon dioxide[13] were found, in addition to pyrrole, at the end of the reaction which supports the intermediacy of the Münchnone in pyrrole formation. Finally, high yields of pyrrole could be formed from either **1a** or **1b** by first reacting the carbene complex with CO in the absence of alkyne and then adding alkyne to the yellow Münchnone solution.

Carbenes **1a** and **1b** reacted with other alkynes, using either initial addition of alkyne or adding alkyne to the preformed Münchnone, and typical results are shown in eq 3. In concert with literature precedent from the work of Huisgen,[14] electron rich or sterically demanding alkynes are not efficient traps of Münchnones. Isolation of sensitive acylaminocarbene complexes can be avoided entirely by using a one-pot procedure of sequential addition of base, acid chloride, and alkyne to transform simple, stable aminocarbene complexes directly to pyrroles (eq 4). Complex **3b** leading to pyrrole **2f** also demonstrates that the thermal CO insertion is not limited to aryl carbene complexes.



(3)

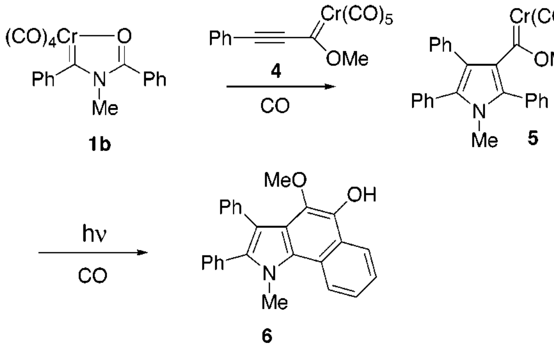
Carbene	R$_1$, R$_2$	Pyrrole
1b	COOMe, COOMe	**2a** 90%
1b	Bu, COOMe	**2b** 36%
1b	H, COOMe	**2c** 80%
1b	Ph, Ph	**2d** 12%
1a	H, Bu	**2e** 27%



(4)

2a R = Ph 72%
2f R = Bu 23%

Since unsaturated carbene complexes are quite efficient reactants in Diels Alder cycloaddition reactions[15] and there have been a few reports of participation in dipolar cycloaddition reactions,[16] we tested the idea of a carbene complex as the dipolarophile to trap the carbene-generated Münchnone.[17] Reaction of complex **1b** with complex **4** under 30 psi CO in the dark for just 2.25 h resulted in complex **5** in 65% yield (eq 5). An important point is that the direct nonphotochemical carbonyl insertion is critical in this instance as, in general, *methoxy*-substituted carbene complexes are more photochemically reactive than *amino*-substituted carbene complexes.[1] Using complex **5** as a substrate in our photochemical benzannulation reaction,[18] photolysis led regioselectively to indole **6** in 51% yield.



(5)

The mechanism broadly outlined in eq 1 is our working framework for pyrrole formation. First, chelated complexes such as **1b** would be converted to the pentacarbonyl complex which should be more reactive toward CO insertion.[4c] Then, direct CO insertion, without photolysis, occurs providing a ketene complex. This is an unusual step since while CO insertion readily occurs with chromium carbene complexes lacking a heteroatom substituent directly bonded to the carbene carbon as part of the Dötz reaction,[2] CO insertion in heteroatom-substituted chromium carbene complexes has been shown in general to be a photochemical, and not thermal, process.[1,3] The acyl substituent must be crucial for reducing electron donation from the nitrogen atom to the carbene carbon and thus activating CO insertion. The ketene cyclizes to a metal-free Münchnone as evidenced by our isolation of 3-methyl-2,4-diphenyl-1,3-oxazolium-5-oxide. The demetalation is likely to be facilitated by the presence of CO. The subsequent alkyne cycloaddition and carbon dioxide cycloreversion are well established and supported by our detection of carbon dioxide.[6] This proposal is in marked contrast with one put forth by Dötz and co-workers[7h] for pyrrole formation from an acylamino molybdenum carbene complex wherein initial alkyne insertion was followed by carbonyl insertion and ketene rearrangement to a 2-alkoxy pyrrole. However, in our chromium case, carbonyl insertion clearly precedes alkyne incorporation.

In summary, we have demonstrated the direct, nonphotochemical, insertion of carbon monoxide in acylamino chromium carbene complexes, formation and trapping of Münchnones, and the use of alkynyl carbene complexes as efficient and functional traps of Münchnones for subsequent benzannulation reactions.

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for support of our work. C.A.M. is a recipient of a Camille Dreyfus Teacher-Scholar (1994–1999) award. A.B. is a recipient of a Deutsche Forschungsgemeinschaft postdoctoral fellowship. C.C.A. is a recipient of National Institutes of Health training grant support and support from the Rohm and Haas Company.

Supporting Information Available: Description of syntheses and characterization data for compounds **1a**–**b**, **2a**–**f**, **5**, **6**, and 3-methyl-2,4-diphenyl-1,3-oxazolium-5-oxide (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) See Supporting Information.

(13) Hexacarbonylchromium was isolated in 49% yield. Carbon dioxide was trapped with an aqueous barium hydroxide solution as barium carbonate in 88% yield.

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