Photolytic Reactions of Chromium Aminocarbene Complexes. Conversion of Amides to α-Amino Acids

Louis S. Hegedus,* Mark A. Schwindt, Stéphane De Lombaert, and Rene Imwinkelried

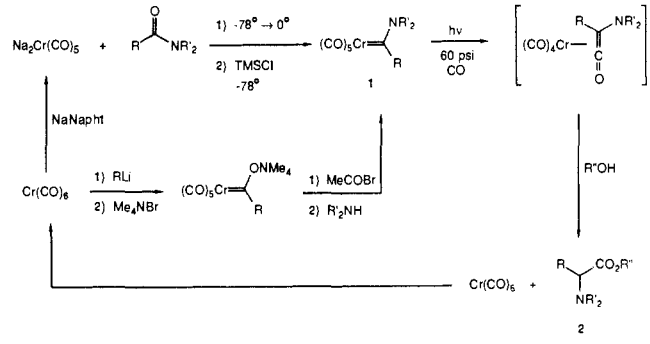
Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. *Received July 27, 1989*

Abstract: A variety of tertiary amides was converted to chromium aminocarbene complexes by reaction with $Na_2Cr(CO)_5$ and trimethylsilyl chloride. Photolysis of these carbene complexes in methanol or *tert*-butyl alcohol solvent produced α-amino esters in good to excellent yield. Aminocarbene complexes containing chiral oxazolidine groups were synthesized and photolyzed in alcohol to produce chiral α-amino esters in 50–93% de. Pentacarbonyl[(dibenzylamino)(methyl)carbene]chromium(0) was prepared in high yield by the N-benzylation of the corresponding monobenzyl amino complex. Base-assisted alkylation of the methyl group with a variety of halides followed by photolysis in methanol produced the alkylated alanine methyl ester in excellent overall yield. Other aminocarbene complexes underwent similar reactions. With chiral, optically active aminocarbene complexes, the alkylated alanine derivative was produced with high diastereoselectivity.

α-Amino acids[1] currently occupy a prominent position in organic chemistry, not only because of their central biological role as the fundamental units of peptides and proteins[2] but also because of their expanding role in pharmaceutical and agricultural chemistry and their utility in the synthesis of optically active compounds.[3] New synthetic approaches to this class of compounds abound.[4] These approaches include asymmetric catalytic hydrogenation of dehydroamino acids,[5] alkylation of electrophilic[6] and nucleophilic glycine derivatives, and nucleophilic and electrophilic amination of carboxylic acid derivatives.[7]

Recent research in these laboratories has centered on the development of useful organic synthetic methodology based on the photolytic reactions of heteroatom-stabilized chromium carbene complexes. The methods developed include the efficient conversion of imines to β-lactams[8] and olefins to cyclobutanones.[9] Photolysis of chromium carbene complexes was shown to generate ketenes or metal-bound ketenes[10] which could be trapped by a variety of nucleophiles including imines (to give β-lactams), olefins, amines, and alcohols.[11] Concurrent with these studies, an efficient synthesis of aminocarbene complexes from amides was developed.[12] Since photolysis of aminocarbene complexes in the presence of alcohols produces α-amino acid esters, combination of these two processes would result in the overall conversion of amides to α-amino acid derivatives, a conversion difficult to achieve with use of conventional organic synthetic methodology. Herein we report the results of studies directed to this end.

Scheme I



Results and Discussion

The general approach to α-amino esters developed is summarized in Scheme I. To be generally useful both the synthesis of the aminocarbenes and the photolytic cleavage by alcohols must be efficient. Aminocarbene complexes can be made by several routes. Potentially, the most general is that recently developed in these laboratories[12] involving the reaction of amides with $Na_2Cr(CO)_5$ and trimethylsilyl chloride (Scheme I). Virtually all formamides and many alkyl amides undergo this transformation in high yield. Many lactams, including β-lactams, are converted to cyclic aminocarbene complexes (e.g., **1f–1l**). However, as the amide carbonyl group becomes more sterically encumbered, the yield of this reaction, when carried out under the reported conditions, drops dramatically. Thus, carbenes **1j** and **1l**, from *N*-benzylpiperidin-2-one and *N*-benzyl-2-azacyclotridecanone, respectively, were produced in only 1–2% under standard conditions. These yields were raised substantially (to 18% for **1j** and 36% for **1l**) by reducing the amount of $Na_2Cr(CO)_5$ used to 1.3–1.5 equiv/equivalent of lactam, by increasing the concentration at which the reaction was run 3-fold, and by extending the reaction time after addition of TMSCl by slowly warming the reaction mixture to −25 °C and holding it at that temperature for 1 h before addition of alumina.

Even under these optimized conditions, some amides failed to convert to the desired aminocarbene. For example, diphenylformamide failed to convert to the desired carbene complex with $Na_2Cr(CO)_5$ under all conditions tried, probably because the addition is an equilibrium process and with sterically hindered amides the tetrahedral intermediate is strongly disfavored (eq 1). Furthermore, the diphenylamine is a reasonable leaving group, the loss of which would produce an unstable formyl complex which would ultimately decompose. With diphenylformamide these

(1) For reviews see: (a) Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816. (b) *Chemistry and Biochemistry of Amino Acids*; Barrett, G. C., Ed.; Chapman and Hall: London, 1985. (c) Greenstein, J. P.; Winitz, M. *Chemistry of the Amino Acids*; R. E. Krieger: FL, 1984; Vol. 1–3.

(2) (a) Bodansky, M. *Principles of Peptide Synthesis*; Springer, Verlag: New York, 1984. (b) Bodansky, M.; Bodansky, A. *The Practice of Peptide Synthesis*; Springer Verlag: New York, 1984.

(3) Copola, G. M.; Schuster, H. F. *Asymmetric Synthesis: Construction of Chiral Molecules Using Amino Acids*; Wiley-Interscience: New York, 1987.

(4) For an overview of recent activity in α-amino acid synthesis, excluding asymmetric hydrogenation of dehydroaminoacids, see: *Tetrahedron Symposia in Print Number 33*; O'Donnell, M. J., Ed.; (*Tetrahedron* **1988**, *44*, 5253–5614) Pergamon Press: Oxford, 1988.

(5) For key references see: *Asymmetric Synthesis, Chiral Catalysts*; Morrison, J. D.; Ed. Academic Press: Orlando, FL, 1985; Vol. 5.

(6) Williams, R. M.; Sinclair, P. J.; Zhai, D.; Chen, D. *J. Am. Chem. Soc.* **1988**, *110*, 1547 and extensive references cited therein.

(7) References 4 and 6 thoroughly cover the current literature dealing with these synthetic approaches, and the references contained therein should be consulted for specific details.

(8) (a) Borel, C.; Hegedus, L. S.; Krebs, J.; Satoh, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1101. (b) Hegedus, L. S.; D'Andrea, S. *J. Org. Chem.* **1988**, *53*, 3113.

(9) Sierra, M.; Hegedus, L. S. *J. Am. Chem. Soc.* **1989**, *111*, 2335.

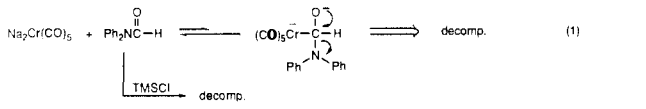
(10) For a review on metal ketene complexes see: Geoffroy, G. L.; Bassner, S. L. *Advances in Organometallic Chemistry*; Academic Press, Inc.: San Diego, CA, 1988; Vol. 28, p 1.

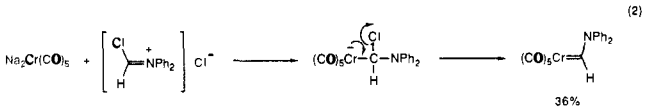
(11) Hegedus, L. S.; deWeck, G.; D'Andrea, S. *J. Am. Chem. Soc.* **1988**, *110*, 2122.

(12) Imwinkelried, R.; Hegedus, L. S. *Organometallics* **1988**, *7*, 702.

0002-7863/90/1512-2264$02.50/0

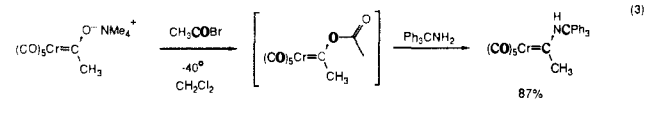
problems could, in part, be circumvented by prior activation of the amide by formation of its Vilsmeir's salt (eq 2).[13] In this





case, the combination of a more electrophilic carbonyl carbon and a good leaving group (Cl^-) is sufficient to permit the reaction to proceed. However, Vilsmeir's salts are sometimes difficult to prepare and purify and often unstable. In contrast, *N,N*-dialkylcarboxamides readily undergo reaction with trimethylsilyl triflate to give stable, easily isolated *N,N*-dialkyl(trimethylsiloxy)methyleneaminium salts[14] and with methyl triflate to give the corresponding methoxy salts. Reaction of these substrates with $Na_2Cr(CO)_5$ to form aminocarbene complexes is currently being developed.

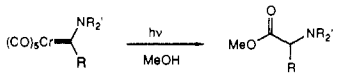
Aminocarbene complexes were first prepared by exchange reactions of amines with alkoxycarbene complexes.[15] However, this process is restricted to primary amines or nonhindered secondary amines such as dimethylamine. Thus, (dibenzylamino)(methyl)carbene **1a** could *not* be prepared by the reaction of dibenzylamine with the (methoxy)(methyl)carbene complex, although the less hindered isoindoline exchanged readily to produce carbene **1b**. Considerably more reactive toward alkoxy exchange reactions are *O*-acylcarbene complexes, produced by the acylation of the tetramethylammonium (but *not* lithium) acylate complexes, usually by acetyl chloride.[16] While this process is efficient with relatively stable *O*-acetylcarbenes (such as the 2-furylcarbene)[17] or with relatively weak nucleophiles such as alcohols,[18] amination of relatively unstable *O*-acetoxycarbenes by sterically hindered amines was not efficient. Preliminary ^1H NMR studies in these laboratories have shown that the more reactive acylating reagent, acetyl bromide, undergoes instantaneous reaction with tetramethylammonium acylate complexes to produce the acetoxycarbene complex in situ with essentially quantitative conversion. Addition of amines to these solutions followed by slow warming produces aminocarbene complexes in much better yield than other exchange routes. By this process (dibenzylamino)methylcarbene complex **1a** and even the very sterically hindered (*N*-tritylamino)carbene complex (eq 3) could be made efficiently.

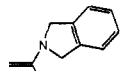
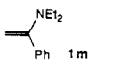
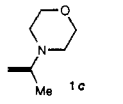
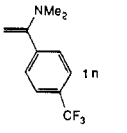
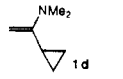
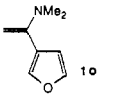
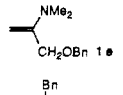
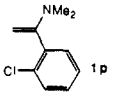
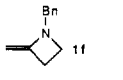
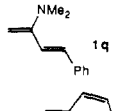
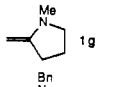
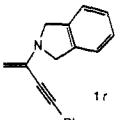
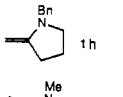
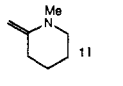
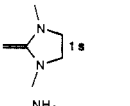
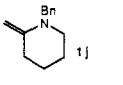
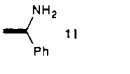
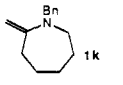


With several approaches to a variety of aminocarbene complexes at hand, photolytic conversion to α-amino esters was next addressed. Photolysis (through Pyrex) of methanol solutions of these carbenes under 60 psi carbon monoxide pressure produced α-amino esters in good to excellent yield in most cases and regenerated chromium hexacarbonyl, which was recovered (60–70%) and reused. The approach is summarized in Scheme I, and the results are collected in Table I.

Simple (amino)(methyl)carbenes containing dibenzylamine, isoindoline, and morpholine as the amine component (**1a–c**) as well as cyclopropyl- and (benzyloxymethyl)carbenes containing dimethylamino groups (**1d,e**) were converted to the corresponding

Table I. Photolytic Conversion of Chromium Aminocarbene Complexes to α-Amino Esters

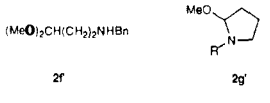


complex **1**	% yield[a]	product, % yield	complex **1**	% yield[a]	product, % yield
 **1a**	44	**2a**, 87[b]	 **1l**	36	**2l**, 96
1b	57	**2b**, 84	**1m**	91	**2m**, 98
 **1c**	78	**2c**, 98	 **1n**	63[c]	**2n**, 88
 **1d**	43	**2d**, 85	 **1o**	96	**2o**, 76
 **1e**	50	**2e**, 82	 **1p**	60	
 **1f**	35	**2f**, 45	 **1q**	20	
 **1g**	98		 **1r**	48[c]	
 **1h**	49				
 **1i**	97	**2i**, 90	 **1s**	94[d]	
 **1j**	32	**2j**, 90	 **1t**	96[e]	**2t**, 84[b]
 **1k**	29	**2k**, 58			

[a] Reported yields are for isolated, purified compounds. [b] *tert*-Butyl alcohol used to produce *tert*-butyl ester. [c] Made by amine exchange from the corresponding methoxycarbene. [d] Made from chromium hexacarbonyl and the corresponding olefin. [e] Made from the methoxycarbene by exchange with ammonia.

α-amino ester in high yield under these conditions. This indicates that these (dialkylamino)alkylcarbenes underwent efficient photochemical CO insertion to form the ketene complex, notwithstanding their failure to react efficiently with imines to give β-lactams under similar conditions.[13] *tert*-Butyl alcohol was also an efficient trap, producing easily cleaved *tert*-butyl esters in excellent yield (**2a**).

Cyclic aminocarbenes (prepared from lactams) with ring sizes of six, seven, and thirteen (**1i–l**) underwent photolysis in methanol to give the corresponding α-amino esters **2i-l** in fair to excellent yield. The four-membered cyclic carbene **1f** underwent reaction much more slowly and gave only modest yields of α-amino ester **2f**. In addition, an almost equal amount of acetal **2f'**, the *formal*



2f' 2g'

product of insertion of the carbene into the O–H bond of methanol, followed by methanolysis, was obtained.[19] The five-membered cyclic aminocarbene complexes **1g** and **1h** were consumed only

(13) Hafner, A.; Hegedus, L. S.; deWeck, G.; Hawkins, B.; Dötz, K. H. *J. Am. Chem. Soc.* **1988**, *110*, 8413.
(14) Ende, H.; Domsch, D.; Feger, H.; Frick, U.; Götz, A.; Hergott, H. H.; Hofmann, K.; Kober, W.; Krägeloh, K.; Oesterle, T.; Steppan, W.; West, W.; Simchen, G. *Synthesis 1982*, 1.
(15) Connor, J. A.; Fischer, E. O. *J. Chem. Soc. A* **1969**, 578.
(16) Fischer, E. O.; Selmazr, T.; Kreissl, F. R. *Chem. Ber.* **1977**, *110*, 2947.
(17) Connor, J. A.; Jones, E. M. *J. Chem. Soc. A* **1971**, 3368.
(18) Semmelhack, M. F.; Bozell, J. J. *Tetrahedron Lett.* **1982**, *23*, 2931.
(19) Acetal formation from formal carbene insertion into an O–H bond has been previously noted: Dötz, K. H. *Naturwissenschaften* **1975**, *62*, 365.

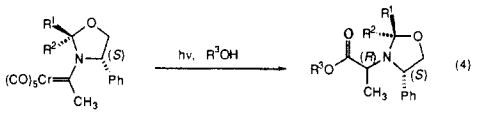
very slowly (4 days for **1h** and 9 days for **1g** vs 2 days for **1i**) and produced *no* identifiable amino ester. Instead, a complex mixture of unidentified materials was produced by photodegradation of the carbene. Amongst these, methanol insertion product **2g'** was tentatively identified by spectroscopic techniques but could not be separated from the mixture. These same two carbenes have unusual spectroscopic properties[13] when compared with those for **1i** (λ_{max} = 351 nm vs 360 nm; δ^{53}Cr = 54 and 77 vs 153), a fact which may be related to their photochemical inertness.

Aromatic aminocarbene complexes also underwent efficient photolysis reaction with methanol. Photolysis of the phenyl- (**1m**), (*p*-(trifluoromethyl)phenyl)- (**1n**) and 3-furyl- (**1o**) carbenes produced the corresponding aryl amino esters **2m–o** in excellent yield. In contrast, photolysis of the (*o*-chlorophenyl)carbene **1p** produced none of the desired amino ester. Among many unidentified products, a small amount of *o*-chlorobenzaldehyde (from hydrolysis of the undetected mixed acetal from carbene insertion into methanol, analogous to **2f'** and **2g'**) was detected. Similarly, photolysis of α,β-unsaturated carbene **1q** produced *no* α-amino ester, although the carbene was consumed within 18 h. A *major* byproduct was cinnamaldehyde, from *apparent* methanolysis of the carbene to give the mixed acetal, followed by hydrolysis to the aldehyde. No products resulting from CO insertion were detected. Although acetylenic carbene complex **1r**, (prepared by exchange) required photolysis for several days to be consumed, it likewise produced a number of unidentified compounds, none of which contained a carbonyl group, indicating that productive CO insertion into this carbene complex was also unsuccessful. Finally, bis aminocarbene **1s** was virtually inert to photolysis in alcohol, and a substantial amount of it remained even after 20 days of photolysis. Since carbenes of this type have exceptionally inert metal–carbon bonds,[20] this lack of reactivity is not surprising.

All of the amino esters produced above contain dialkylamino groups, since the reaction of $Na_2Cr(CO)_5$ with amides to produce aminocarbenes is restricted to tertiary amides. However, aminocarbene complexes are also readily available by exchange reactions (Scheme I) and both free amino- and monoalkylaminocarbenes are available by this route. These aminocarbenes also are readily converted to α-amino esters by photolysis in alcohol (e.g., **1t** to **2t**).

Surprisingly, preliminary attempts to generate free amino acids directly by photolysis of aminocarbene complexes in the presence of water (aqueous THF or CH_3CN) have failed. In the presence of water the photolysis takes a totally different route and produces a mixture of compounds, none of which are the amino acid.

Since the synthesis of optically active α-amino acids is of current interest,[4] induction of asymmetry in this process was briefly examined. Aminocarbene complexes bearing a chiral oxazolidine ring as the heteroatom substituent have recently been synthesized in these laboratories[12] by the reaction of the corresponding formamide with $Na_2Cr(CO)_5$ and have been shown to be efficient in the synthesis of optically active β-lactams.[21] Related carbenes from acetamides of chiral oxazolidines proved more difficult to prepare. The least sterically hindered complex **3a** (eq 4) could



3a R = R² = H
3b R¹ = iPr; R² = H
3c R¹ = R² = Me

4a R³ = Me 86% (70% de)
4b R³ = Me 96% (70% de)
4b' R³ = tBu 81% (42% de)
4c R³ = Me 96% (≥93% de)
4c' R³ = tBu 77% (≥93% de)

be prepared from the corresponding acetamide and $Na_2Cr(CO)_5$, giving a separable 3:1 mixture of rotamers about the carbene–carbon–nitrogen bond in low yield (24%). Photolysis of each of these rotamers in methanol gave equal, excellent yields of the amino ester **4a** but with only modest (70%) diastereomeric excess. The more sterically hindered carbenes **3b** and **3c** could not be prepared from the corresponding acetamides, and the alternative exchange process had to be used. Carbene **3b** was obtained in low (unoptimized, 13%) yield, while **3c** was obtained in somewhat better (unoptimized 31%) yield. In both cases a single rotamer was obtained, after purification. (Both rotamers may have been formed, and one was lost during purification. The presence of paramagnetic impurities in the mixture before purification precluded NMR spectroscopic analysis.) Photolysis of **3b** in both methanol and *tert*-butyl alcohol, under a carbon monoxide atmosphere produced α-amino esters **4b** and **4b'** in excellent chemical yield. However, diastereoselectivity was poor and was dependent on the alcohol used as the trapping agent. Of the three oxazolidine chiral auxiliaries studied, **3c** (derived from *S*-phenyl glycinol and acetone) was the most efficient. Photolysis in methanol under carbon monoxide produced an excellent yield of amino ester **4c** as a single diastereoisomer, within the limits of detection. With *tert*-butyl alcohol under an argon atmosphere, the yield of ester **4c'** was slightly lower, but again only a single diastereoisomer was detected. For unknown reasons, when this same reaction was carried out under a carbon monoxide atmosphere slightly lower chemical and stereochemical yields were obtained (68% yield, ~90% de). The absolute stereochemistry of the newly formed stereogenic center was shown to be *opposite* that of the chiral auxiliary by removal of the chiral auxiliary by published procedures (hydrolysis/hydrogenolysis/hydrolysis).[22]

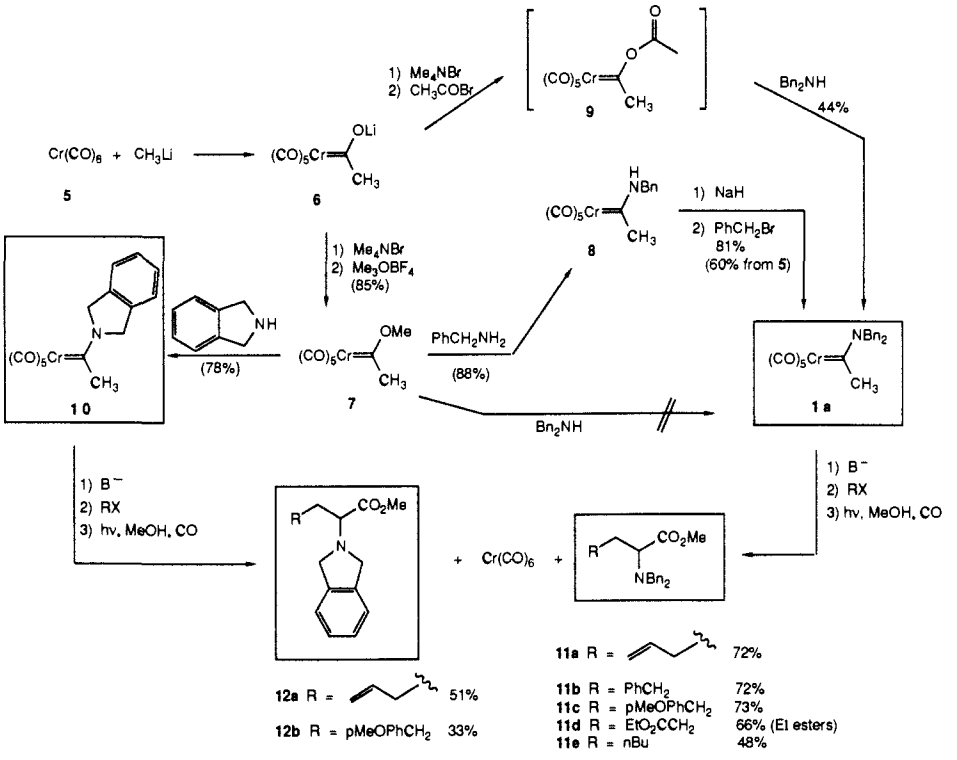
The major limitations to the complexity of the α-amino esters available by this route lie in the intrinsic difficulties in preparing the requisite sterically hindered or sensitively functionalized carbene complexes, which, in turn, are the result of fundamental limitations in the conventional synthetic approaches to these carbenes. Aminocarbene complexes are generally prepared either by the aminolysis of acetoxy- or alkoxycarbene complexes or by the reaction of tertiary amides with $Na_2Cr(CO)_5$ and trimethylsilyl chloride.[12] The aminolysis route suffers two limitations. Since the R group is organolithium-derived, very few functional groups are tolerated in this portion of the complex. Since only sterically nonhindered (preferentially primary) amines exchange efficiently, the range of structural features in the amine portion of the complex is similarly restricted. The dianion/amide route has similar limitations. Sterically hindered tertiary amides produce only modest yields of the desired carbene complex. Since the dianion is a strong base, a strong nucleophile, and a strong reducing agent, the range of compatible functional groups in the amide is similarly limited.

An ideal synthesis of aminocarbene complexes would permit the large scale, high yield synthesis of a wide variety of functionalized carbene complexes starting from a simple, readily available precursor in a minimum number of steps. Attempts to achieve such a synthesis by the efficient preparation of (dibenzylamino)(methyl)carbene **1a**, base-assisted α-alkylation, and direct photolysis without purification to produce α-amino esters are summarized in Scheme II.

(Methoxy)(methyl)carbene **7** is easily prepared on a multigram scale in excellent yield,[30] by the normal Fischer procedure or from

(20) (a) Hitchcock, P. B.; Lappert, M. F.; Pye, P. L. *J. Chem. Soc., Dalton Trans.* **1977**, 2160. (b) Anderson, D. M.; Bristow, G. S.; Hitchcock, P. B.; Jason, H. A.; Lappert, M. F. *J. Chem. Soc., Dalton Trans.* **1987**, 2843.
(21) Hegedus, L. S.; Imwinkelried, R.; Alarid Sargent, M.; Dvorak, D.; Satoh, Y. *J. Am. Chem. Soc.* In press.
(22) Harada, K.; Tamura, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1227.
(23) Kopecky, J.; Smejkal, J. *Chem. Ind.* **1966**, 1529.
(24) *The Chemistry of Amides*; Beckwith, A. L. J., Zabicky, J., Ed.; Interscience: New York, 1970; pp 73–185.
(25) Wasserman, H. H.; Hlasta, D. J.; Tremper, A. W.; Wu, J. S. *Tetrahedron Lett.* **1979**, 549.
(26) Meyers, A. I.; Kunnen, K. B.; Still, W. C. *J. Am. Chem. Soc.* **1987**, *109*, 4405.
(27) This material was identical in all respects with that prepared by the aminolysis method.[13]
(28) All spectroscopic evidence corresponds to the following: (a) Kingsbury, C. A.; Soriano, D. S.; Podroza, K. F.; Cromwell, N. H. *J. Heterocycl. Chem.* **1982**, *19*, 89. (b) Rodebauch, R. M.; Cromwell, N. H. *J. Heterocycl. Chem.* **1968**, *5*, 309.
(29) All spectroscopic data match that reported: Koskinen, A. *Tetrahedron* **1983**, *39*, 1627.
(30) Hegedus, L. S.; McGuire, M. A.; Schultze, L. M. *Org. Synth.* **1987**, *65*, 140.

Scheme II



the reaction of the (commercially available)[31] tetramethylammonium salt of **6** with trimethyloxonium tetrafluoroborate. Dibenzylamine does *not* directly displace the methoxy group from **7**. However, monobenzylamine undergoes exchange in very high yield producing **8**,[32] which is readily N-alkylated by treatment with sodium hydride followed by benzyl bromide,[33] producing the desired complex **1a** in overall 60% yield from chromium hexacarbonyl. This same carbene complex **1a** is also available via the *O*-acetyl (complex **9**) exchange route or by the reaction of dibenzyl acetamide with $Na_2Cr(CO)_5$.[12] However, in spite of requiring more steps, the route to **1a** via **8** is the most convenient to carry out on a large scale and has the best overall yield (60% vs 40–45%). Isoindoline, a dibenzylamine analogue, is much less sterically hindered and readily displaces the methoxy group from **7**, producing isoindoline complex **10** in excellent yield.[34] With these appropriate, simple aminocarbene complexes readily available on a large scale in good yield, elaboration via α-carbanion chemistry was next addressed.

The α-protons on the alkyl group of (methoxy)(alkyl)carbene complexes such as **7** are very acidic[35] and are easily removed by a variety of bases. The resulting stabilized carbanions undergo alkylation reactions with reactive electrophiles such as activated halides or triflates[36] and aldol type condensation with aldehydes in the presence of Lewis acids[37] or trimethylsilyl chloride.[38] (Amino)(alkyl)carbene complexes such as **1a** or **10** should be substantially less acidic than the corresponding alkoxycarbenes, and the resulting α-anions considerably more reactive (e.g., CH_2CO_2R vs CH_2CONR_2). Indeed, the (dimethylamino)methyltungsten carbene complex underwent efficient Peterson olefination by sequential deprotonation with butyllithium, reaction of the resulting α-anion with trimethylsilyl chloride, deprotonation, and condensation with aldehydes or ketones.[39] Very recently α-anions of chromium aminocarbene complexes were shown to undergo aldol condensation reactions.[40]

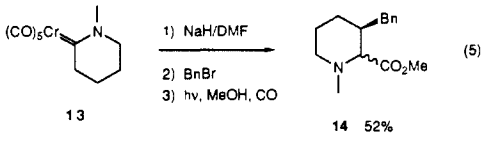
Chart I

Thus, as anticipated, aminocarbene complex **1a** was readily α-deprotonated by butyllithium in THF, potassium bis(trimethylsilyl)amide in THF/toluene, or by sodium hydride in DMF, and the resulting α-carbanions were reactive toward a range of organic halides, including allylic and benzylic bromides, α-bromo esters, and even *n*-butyl bromide (slow, incomplete conversion) and iodide. Although the resulting α-alkylated carbene complexes could be isolated if desired, for the synthesis of α-amino acid esters it proved more efficient to simply dissolve the crude α-alkylation product in methanol and photolyze under a modest (60 psi) pressure of carbon monoxide. This procedure provided functionalized α-amino esters in excellent overall yield with a minimum amount of experimental manipulation (Scheme II, compounds **11**). In addition, the starting chromium hexacarbonyl precipitated from the reaction solution and could be recovered and reused. This procedure constitutes a five-step conversion of $Cr(CO)_6$ and methyllithium to a range of α-amino esters in *overall* 45–55% yield. The α-anion of complex **1a** is a synthetic analogue of the *homoenolate*[41] of alanine (Chart I) and should prove generally useful for the synthesis of homoalanine derivatives not readily accessible by conventional synthetic methodology. Although the isoindoline complex **10** was also readily carried through this sequence, the α-amino esters **12** were quite air sensitive and difficult

(31) Aldrich Chemical Company, compound 34264-5.
(32) Connor, J. A.; Fischer, E. O. *J. Chem. Soc.* **1969**, 578.
(33) (a) Moser, E.; Fischer, E. O. *J. Organomet. Chem.* **1968**, *15*, 147. (b) Casey, C. P.; Vollendorf, N. W.; Haller, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 3754. (c) Parker, A.; Rudler, H.; Daran, J. C.; Alvarez, C.; Delgado, Reyes, F. *J. Organomet. Chem.* **1987**, *327*, 339.
(34) Hafner, A.; Hegedus, L. S.; deWeck, G.; Hawkins, B.; Dötz, K. H. *J. Am. Chem. Soc.* **1988**, *110*, 8413.
(35) (a) Kreiter, C. G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 390. (b) Casey, C. P.; Anderson, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 1230.
(36) Xu, Y.-C.; Wulff, W. D. *J. Org. Chem.* **1987**, *52*, 3263 and extensive references therein.
(37) Wulff, W. D.; Gibertson, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 507.
(38) Aumann, R.; Heinan, H. *Chem. Ber.* **1987**, *120*, 537.
(39) Macromber, D. W.; Madhakur, P.; Rogers, R. D. *Organometallics* **1989**, *8*, 1275.
(40) Wulff, W. D.; Anderson, B. A.; Toole, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 5485. After submission of this paper, Wulff reported a similar α-alkylation of aminocarbene complexes: Wulff, W. D.; Anderson, B. A.; Isaacs, L. D. *Tetrahedron Lett.* **1989**, *30*, 4061.
(41) For alanine homoenolate equivalents see: Jackson, R. F. W.; James, K.; Wythes, J. M.; Wood, A. *J. Chem. Soc., Chem. Commun.* **1989**, 644 and references therein.

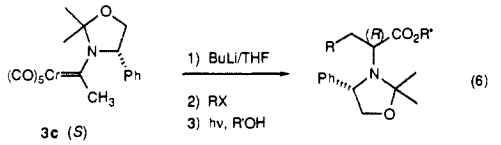
to purify without losses due to air oxidation of the product. (Even simple isoindolines readily air oxidize, turning red, then black, within hours of exposure to air.) Hence, although the crude yields of ester were excellent, the compounds decomposed during and after purification and are of little use synthetically.

This α-alkylation–photolysis process is not restricted to simple (amino)(methyl)carbene complexes. Cyclic carbene complex **13** underwent this two-step process smoothly, producing the benzylated pipecolic ester derivative **14** in good yield, as a 1:1 mixture of diastereoisomers (eq 5).



13 14 52% (5)

Chiral, optically active (*S*) aminocarbene complex **3c** also underwent this α-alkylation/photolysis process, producing chiral, optically active homoalanine derivatives **15a**, **15b** in fair yield and with excellent diastereoselectivity (eq 6). The somewhat lower



3c (S) (6)

15a R = $PhCH_2$, R^1 = tBu, 42% yield, ≥ 93% de

15b R = $tBuO_2CCH_2$, R^1 = Me, 52% yield, ≥ 93% de

chemical yields experienced with complex **3c** were primarily due to the relative instability of the anion, with yields of the alkylation step being ~70%. Improvements of this process and applications of this methodology to the synthesis of unusual optically active amino acids are under study.

Experimental Section

General Procedures. Melting points were taken on a Mel-Temp apparatus and are uncorrected. A Bruker IBM 200 NMR spectrometer was used for the 200 MHz ^1H NMR spectra. The 270 MHz ^1H NMR and the 67 MHz ^{13}C NMR spectra were obtained in a Bruker IBM 270 NMR spectrometer. NMR spectra were recorded in $CDCl_3$, and chemical shifts are given in ppm relative to Me_4Si (0 ppm, ^1H) or $CDCl_3$ (77 ppm, ^{13}C) unless otherwise specified. Assignments in the ^{13}C NMR spectra (broad band) are based on comparison in the measured substance class. IR spectra were recorded on a Beckmann 4240 spectrophotometer. Electron impact (EI) and chemical ionization (CI) mass spectra were obtained on a V. G. Micromass Ltd., Model 16F spectrometer. A Varian Techtron Model 635 or a Perkin-Elmer Lambda 4B UV–vis spectrophotometer was used for the UV spectra. Optical rotations were obtained on a Perkin-Elmer 24 polarimeter at a wavelength of 589 nm (sodium D line) by a 1.0-dm cell with a total volume of 1 mL. Specific rotation, $[\alpha]_D$, was reported in degrees per decimeter at the specified temperature and the concentration (c), given in grams per 100 mL in the specified solvent.

For the purification of crude reaction mixtures, radial-layer (Chromatotron Model 7924) and column chromatographic techniques were applied in most cases. Merck silica gel 60 PF (for radial-layer chromatography) and Merck silica gel (230–400 mesh) or Alfa activated, neutral aluminum oxide (for column chromatography) were used as stationary phases.

Elemental Analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Materials. Tetrahydrofuran (Fisher, reagent grade) and diethyl ether (ASP, analytical reagent) were predried over CaH_2 and distilled from benzophenone ketyl under a nitrogen atmosphere just prior to use. Hexane (technical grade) was distilled at atmospheric pressure. Ethyl acetate (technical grade) was distilled at atmospheric pressure from CaH_2. Methylene chloride was distilled over CaH_2 or filtered through aluminum oxide (Baker Analyzed, 5 g/100 mL). Acetonitrile (Fisher) was distilled over CaH_2 and stored over 4 Å molecular sieves. Methanol (Fisher) was dried over Mg and distilled.

Preparation of Amides. The amide precursors to carbene complexes **1c**, **1d**,[23] **1e**, **1m**, **1o**, **1p**, and **1q** were prepared by literature methods.[12] The amide precursors to carbene complexes **1a** and **1b** were prepared from the corresponding acid chloride and the appropriate amine, following the general procedure reviewed by Beckwith.[24] The *N*-benzylazetidinone was prepared by a solid phase catalyzed ring closure of the β-bromo-*N*-benzlpropionamide.[25] The remaining *N*-benzyl lactams **1h**, **1j**, **1k**, and **1l** were prepared from the corresponding lactam by the N-benzylation procedures of Meyers.[26]

Preparation of Aminocarbene Complexes. The carbene complexes **1b**, **1c**, **1d**, **1e**, **1g**, **1i**, **1m**, **1o**, **1p**, and **1q** were prepared by the method of Imwinkelried.[12] The amount of $Na_2Cr(CO)_5$ could be reduced from 2 equiv/equiv of amide to 1.2–1.5 without effecting the yield.

Pentacarbonyl[(*N*-isoindolinyl)(methyl)carbene]chromium(0) (1b). From 17.3 mmol $Na_2Cr(CO)_5$ and 1.40 g (8.7 mmol) of *N*-isoindoline acetamide 1.92 g (57%) of **1b** as a cream-colored crystalline solid was obtained.[27]

Pentacarbonyl[(*N*,*N*-dimethylamino)(cyclopropyl)carbene]chromium(0) (1d). From 20.0 mmol of $Na_2Cr(CO)_5$ and 1.13 g (10.0 mmol) of *N*,*N*-dimethylcyclopropane carboxamide was obtained 1.25 g (43%) of **1d** as a yellow crystalline solid: mp 69–71 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 1.16 (m, 4 H, CH_2), 1.71 (quin, J = 7.4 Hz, 1 H, =CCH), 3.51 (s, 3 H, NCH_3), 3.89 (s, 3 H, NCH_3); ^{13}C NMR (67 MHz, $CDCl_3$) δ 10.8 (CH_2), 32.4 (*C*H), 44.5 (N*C*H_3), 53.0 (N*C*H_3), 217.9 (cis CO), 223.4 (trans CO), 276.0 (Cr=C); IR (film) ν 2044, 1965, 1912, 1862 cm^{-1}; UV-vis (11.7 mg, 250 mL hexane) λ_{max} 336 nm (ϵ = 6389) (sh), 335 nm; ms (EI) m/z 289 (M^+), 261 (M - CO), 232 (M - 2CO), 205 (M - 3CO), 177 (M - 4CO), 149 (M - 5CO). This material was relatively unstable, and acceptable elemental analyses were unobtainable.

Pentacarbonyl(*N*-methyl-2-azacyclohexylidene)chromium(0) (1i). From 20.0 mmol of $Na_2Cr(CO)_5$ and 1.13 g (10.0 mmol) of *N*-methylpiperidin-2-one was obtained 2.79 g (97%) of **1i** as a pale yellow crystalline solid: mp 53 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 1.52 (quin, J = 6.5 Hz, 2 H, CH_2), 1.83 (quin, J = 6.5 Hz, 2 H, CH_2), 3.25 (t, J = 6.5 Hz, 2 H, =CCH_2), 3.47 (t, J = 6.5 Hz, 2 H, NCH_2), 3.78 (s, 3 H, NCH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.0 (CH_2), 22.0 (CH_2), 49.7 (=C*C*H-$_2$), 52.4 (N*C*H_3), 54.5 (N*C*H_2), 218.1 (cis *C*O), 223.3 (trans CO), 269.9 (Cr=C); IR (film) ν 2050, 1965, 1918 cm^{-1}; UV-vis (12.8 mg/250 mL hexane) λ_{max} 360 nm (ϵ = 6953) (sh), 332 nm. Anal. Calcd for $C_{11}H_{11}NO_5Cr$: C, 45.68; H, 3.83; N, 4.84. Found: C, 45.32; H, 4.16; N, 4.74.

Preparation of Complexes 1a, 1f, 1h, 1k. The carbene complexes **1a**,[13] **1f**, **1h**, **1k**, and **3a** were prepared by the above procedure but by using a more concentrated (0.3 M vs 0.1 M) solution of $Na_2Cr(CO)_5$.

Pentacarbonyl(*N*-benzyl-2-azacyclobutylidene)chromium(0) (1f). From 4.96 mmol of $Na_2Cr(CO)_5$ and 0.40 g (2.50 mmol) of *N*-benzylazetidinone was obtained 0.29 g (35%) of **1f** as a yellow crystalline solid: mp 51 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 2.92 (t, J = 3.0 Hz, 2 H, CH_2), 4.13 (t, J = 3.0 Hz, 2 H, NCH_2), 4.88 (s, 2 H, NCH_2Ph), 7.32–7.44 (m, 5 H, ArH); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 42.9 (CH_2), 56.5 (N*C*H_2), 57.2 (N*C*H_2Ph), 128.7, 128.9, 129.3, 132.9, 217.7 (cis CO), 223.3 (trans CO), 288.3 (Cr=C); IR (film) ν 2020, 1965, 1915, 1895 cm^{-1}; UV-vis (11.3 mg/250 mL hexane) λ_{max} 352 nm (ϵ = 7715) (sh), 331 nm. Anal. Calcd for $C_{15}H_{11}NO_5Cr$: C, 53.42; H, 3.29; N, 4.15. Found: C, 53.52; H, 3.49; N, 4.15.

Pentacarbonyl(*N*-benzyl-2-azacyclopentylidene)chromium(0) (1h). From 22.8 mmol of $Na_2Cr(CO)_5$ and 2.00 g (11.4 mmol) of *N*-benzylpyrrolidin-2-one was obtained 1.90 g (49%) of **1h** as a pale yellow crystalline solid: mp 100–103 °C (dec); ^1H NMR (300 MHz, $CDCl_3$) δ 1.85 (quin, J = 7.7 Hz, 2 H, CH_2), 3.43 (t, J = 7.7 Hz, 2 H, =CCH_2), 3.52 (t, J = 7.7 Hz, 2 H, NCH_2), 5.26 (s, 2 H, NCH_2Ph), 7.27, 7.40 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.9 (CH_2), 56.4 (=C*C*-H_2), 58.7 (N*C*H_2), 59.2 (N*C*H_2Ph), 127.8, 128.6, 129.2, 134.0, 218.0 (cis CO), 223.0 (trans CO), 268.1 (Cr=C); IR (film) ν 2050, 1962, 1952, 1895 cm^{-1}; UV-vis (12.9 mg/250 mL hexane) λ_{max} 354 nm (ϵ = 7541) (sh), 330 nm. Anal. Calcd for $C_{16}H_{13}NO_5Cr$: C, 54.71; H, 3.73; N, 3.99. Found: C, 54.84; H, 4.00; N, 3.89.

Pentacarbonyl(*N*-benzyl-2-azacycloheptylidene)chromium(0) (1k). From 19.1 mmol of $Na_2Cr(CO)_5$ and 1.94 g (9.5 mmol) of *N*-benzyl-2-azacycloheptanone was obtained 1.06 g (29%) of **1k** as a clear pale yellow-green oil: ^1H NMR (200 MHz, $CDCl_3$) δ 1.40 (m, 2 H, CH_2), 1.68 (m, 4 H, CH_2), 3.40 (m, 2 H, =CCH_2), 3.62 (m, 2 H, NCH_2), 5.42 (s, 2 H, NCH_2Ph), 7.28, 7.43 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.1 (CH_2), 25.7 (CH_2), 28.8 (CH_2), 52.2 (=C*C*H_2), 53.9 (N*C*H_2), 68.9 (N*C*H_2Ph), 127.8, 128.5, 129.0, 134.3, 217.6 (cis CO), 223.5 (trans CO), 280.6 (Cr=C); IR (film) ν 2040, 1972, 1930 cm^{-1}; UV-vis (9.4 mg/250 mL hexane) λ_{max} 364 nm (ϵ = 7647) (sh), 333 nm. Anal. Calcd for $C_{18}H_{17}NO_5Cr$: C, 56.99; H, 4.51; N, 3.69. Found: C, 57.03; H, 4.62; N, 3.75.

Preparation of Complexes 1j and 1l. The carbene complexes **1j** and **1l** were prepared by using the modification above (increased concentration). In addition the amount of time at each temperature was doubled. After the addition of TMSCl, the reaction mixture was stirred at −78 °C for 1 h, warmed slowly to −25 °C, and stirred for another hour before

addition of Al_2O_3. The solvent was removed, and the product was purified by chromatography on a column as previously described.

Pentacarbonyl(*N*-benzyl-2-azacyclohexylidene)chromium(0) (1j). From 1.1 mmol of $K_2Cr(CO)_5$ and 0.14 g (1.0 mmol) of *N*-benzylpiperidin-2-one was obtained 0.10 g (32%) of **1j** as a pale yellow crystalline solid: mp 87–89 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 1.59 (quin, J = 6.5 Hz, 2 H, CH_2), 1.66 (quin, J = 6.5 Hz, 2 H, CH_2), 3.29 (t, J = 6.5 Hz, 2 H, $=CCH_2$), 3.32 (t, J = 6.5 Hz, 2 H, NCH_2), 5.37 (s, 2 H, NCH_2Ph), 7.25, 7.39 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.6 (CH_2), 21.6 (CH_2), 49.9 ($=CCH_2$), 51.1 (NCH_2), 68.1 (NCH_2Ph), 127.4, 128.4, 129.0, 134.5, 217.8 (cis CO), 223.3 (trans CO), 273.0 (Cr=C); IR (film) ν 2042, 1982, 1922, 1902 cm^{-1}; UV-vis (11.2 mg/250 mL hexane) λ_{max} 360 nm (ε = 6850) (sh), 335 nm. Anal. Calcd for $C_{17}H_{25}NO_5Cr$: C, 55.90; H, 4.14; N, 3.83. Found: C, 56.04; H, 4.22; N, 3.78.

Pentacarbonyl(*N*-benzyl-2-azacyclotridecylidene)chromium(0) (1l). From 30.5 mmol of $Na_2Cr(CO)_5$ and 5.64 g (19.6 mmol) of *N*-benzyl-2-azacyclotridecanone was obtained 3.43 g (36%) of **1l** as a cream-colored crystalline solid which was recrystallized from CH_2Cl_2/hexane for elemental analysis: ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (m, 8 H, CH_2), 1.40 (m, 4 H, CH_2), 1.64 (m, 2 H, CH_2), 1.77 (m, 4 H, CH_2), 3.16 (m, 2 H, $=CCH_2$), 3.41 (m, 2 H, NCH_2), 5.43 (s, 2 H, NCH_2Ph), 7.21, 7.40 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 22.2, 22.4, 23.5, 23.6, 24.2, 24.3, 26.4, 26.5 (CH_2), 50.4 ($=CCH_2$), 50.6 (NCH_2), 66.4 (NCH_2Ph), 127.0, 128.3, 129.1, 135.1, 217.7 (cis CO), 223.1 (trans CO), 281.0 (Cr=C); IR (film) ν 2050, 1975, 1945, 1930, 1895 cm^{-1}; UV-vis (9.6 mg/250 mL hexane) λ_{max} 363 nm (ε = 8340) (sh), 334 nm. Anal. Calcd for $C_{24}H_{29}NO_5Cr$: C, 62.19; H, 6.31; N, 3.02. Found: C, 62.30; H, 6.21; N, 2.95.

Preparation of Complexes 1n, 1r, 1t, and 1s. The carbene complexes **1n**, **1r**, and **1t** were prepared by the amine/methoxy exchange procedure previously reported.[13] Complex **1s** was prepared from $Cr(CO)_6$ and the corresponding olefin.[13]

Pentacarbonyl[((5*S*)-1-aza-3-oxa-5-phenylcyclopentyl)(methyl)carbene]chromium(0) (3a). From 4.1 mmol of $Na_2Cr(CO)_5$ and 0.40 g (2.1 mmol) of the corresponding amide were obtained two separate carbene rotamers in the amount of 136 mg (18%) and 46 mg (6%) as pale yellow crystalline solids: (major rotamer mp 84 °C (dec); $[\alpha]_D$ −25.0° (c = 1, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 2.60 (s, 3 H, CH_3), 4.16 (dd, J = 3.0, 9.0 Hz, 1 H, OCH_2), 4.51 (dd, J = 6.0, 9.0 Hz, 1 H, OCH_2), 5.18 (dd, J = 3.0, 6.0 Hz, 1 H, NCHPh), 5.55 (d, J = 8.0 Hz, 1 H, NCH_2O), 5.80 (d, J = 8.0 Hz, 1 H, NCH_2O), 7.15, 7.41 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 42.1 (CH_3), 65.4 (OCH_2), 75.7 (NCHPh), 88.4 (NCH_2O), 125.5, 128.6, 129.6, 138.0, 217.6 (cis CO), 222.7 (trans CO), 274.4 (Cr=C); IR (film) ν 2045, 1978, 1912, 1895 cm^{-1}; UV-vis (9.1 mg/250 mL hexane) λ_{max} 366 nm (ε = 9061) (sh), 332 nm. Anal. Calcd for $C_{16}H_{13}NO_6Cr$: C, 52.32; H, 3.57; N, 3.81. Found: C, 52.34; H, 3.73; N, 3.76. Minor rotamer: ^1H NMR (300 MHz, $CDCl_3$) δ 2.88 (s, 3 H, CH_3), 4.25 (d, J = 8.8 Hz, 1 H, OCH_2), 4.42 (dd, J = 5.1, 8.8 Hz, 1 H, OCH_2), 5.17 (d, J = 6.5 Hz, 1 H, NCH_2O), 5.39 (d, J = 6.5 Hz, 1 H, NCH_2O), 5.71 (d, J = 4.9 Hz, 1 H, NCHPh), 7.16, 7.40 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.9 (CH_3), 70.1 (OCH_2), 74.6 (NCHPh), 83.5 (NCH_2O), 125.8, 128.4, 129.1, 139.1, 217.1 (cis CO), 222.8 (trans CO), 277.5 (Cr=C).

Pentacarbonyl[((2*R*,5*S*)-1-aza-2-isopropyl-3-oxa-5-phenylcyclopentyl)(methyl)carbene]chromium(0) (3b). The tetramethylammonium salt of [(oxy)(methyl)carbene]pentacarbonylchromium (2.0 g, 6.61 mmol) was dissolved in deoxygenated dichloromethane (40 mL) and cooled to −40 °C under argon. Acetyl bromide (488 μL, 6.61 mmol) was added dropwise. The red solution was stirred during 1 h at −40 °C. A solution of 2(*R*,*S*)-4(*S*)-2-isopropyl-4-phenyl-1,3-oxazolidine was prepared by stirring (*S*)-phenylglycinol (1.09 g, 7.94 mmol), isobutyraldehyde (721 μL, 7.94 mmol), and anhydrous magnesium sulfate (6 g) in dichloromethane (17 mL) at 5 °C for 1 h. ^1H NMR analysis of an aliquot revealed the presence of two diastereoisomers in a 4:1 ratio (absolute configuration not established): ^1H NMR (270 MHz, $CDCl_3$, major isomer) δ 1.04 (d, J = 6.7 Hz, 3 H, CH_3), 1.06 (d, J = 6.7 Hz, 3 H, CH_3), 1.88 (m, 1 H, CH), 2.00 (br s, 1 H, NH), 3.64 (t, J = 7.6 Hz, CHN), 4.12 (t, J = 7.4 Hz, CH_2O), 4.14 (d, J = 6.5 Hz, 1 H, CH_2O), 7.34 (m, 5 H, ArH).

The crude 1,3-oxazolidine solution was concentrated in vacuo, and the residue was redissolved in dichloromethane (2 mL). This solution was added with a syringe at −40 °C to the acetoxycarbene solution. The orange suspension was allowed to warm up slowly overnight. Saturated sodium bicarbonate (20 mL) was added. The aqueous layer was extracted with dichloromethane (20 mL). The combined organic layers were dried on anhydrous magnesium sulfate, filtered through a bed of Celite and silica gel, and concentrated in vacuo. The dark residue was triturated in hexane. The solid was recrystallized from ethyl acetate/hexane to give the desired aminocarbene as yellow prisms (two crops): 367 mg (13.5% based on ammonium salt).

The aminocarbene was obtained as a single diastereoisomer and rotamer. The 2*R* configuration was deduced from differential NOE experiments: mp ≥ 140 °C dec; $[\alpha]_D$ +187.0° (c 1, CH_2Cl_2); ^1H NMR (270 MHz, $CDCl_3$) δ 1.01 (d, J = 6.7 Hz, 3 H, CH_3), 1.26 (d, J = 6.7 Hz, 3 H, CH_3), 2.46 (m, 1 H, CH), 2.83 (s, 3 H, CH_3), 4.24 (dd, J = 6.3, 8.9 Hz, 1 H, CH_2O), 4.70 (t, J = 8.6 Hz, 1 H, CH_2O), 5.33 (m, 1 H, NCHPh), 5.77 (d, J = 7.4 Hz, 1 H, NCHO), 7.08, 7.40 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.1 (CH_3), 18.4 (CH_3), 29.5 (CH), 44.3 ($=CCH_3$), 64.8 (CH_2O), 72.2 (NCHPh), 103.2 (OCHN), 125.2, 128.2, 129.2, 137.4, 218.0 (cis CO), 223.0 (trans CO), 280.5 (Cr=C); IR (film) ν 2052, 1960, 1920, 1891 cm^{-1}. Anal. Calcd for $C_{19}H_{19}NO_6Cr$: C, 55.74; H, 4.68; N, 3.42. Found: C, 55.91; H, 4.71; N, 3.35.

Pentacarbonyl[((5*S*)-1-aza-2,2-dimethyl-3-oxa-5-phenylcyclopentyl)(methyl)carbene]chromium(0) (3c). The tetramethylammonium salt of [(oxy)(methyl)carbene]pentacarbonylchromium (2.6 g, 8.34 mmol) was dissolved in deoxygenated dichloromethane (80 mL) and cooled to −40 °C under argon. Freshly distilled acetyl bromide (616 μL, 8.34 mmol) was added dropwise. The red solution was stirred during 30 min at −40 °C. A solution of 2,2-dimethyl-4-phenyl-1,3-oxazolidine (10.85 mmol) and *N*-methylmorpholine (934 μL, 8.5 mmol) in dichloromethane (5 mL) was added with a syringe. After 30 min at −40 °C, the orange suspension was allowed to warm up slowly to −10 °C during a 2-h period. Neutral alumina (20 g) was added, and the mixture was filtered through Celite. The orange filtrate was concentrated in vacuo. The dark residue was adsorbed on silica gel, dried under high vacuum, and transferred on top of a column filled with silica gel. Elution with hexane allowed the removal of nonpolar impurities. The desired aminocarbene (single rotamer by ^1H NMR) was obtained by eluting with 5% ethyl acetate. Recrystallization from ethyl acetate/hexane afforded the aminocarbene as yellow prisms (two crops): 1.01 g (31% based on the ammonium salt); mp ≥ 112 °C dec; $[\alpha]_D$ −21.8° (c 1, CH_2Cl_2); ^1H NMR (270 MHz, $CDCl_3$) δ 1.76 (s, 3 H, CH_3), 1.84 (s, 3 H, CH_3), 3.16 (s, 3 H, $=CCH_3$), 4.28 (dd, J = 1.0, 8.3 Hz, 1 H, CH_2O), 4.55 (dd, J = 5.1, 8.3 Hz, 1 H, CH_2O), 5.86 (d, J = 5.1 Hz, 1 H, NCHPh), 7.18, 7.38 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.4 (CH_3), 27.9 (CH_3), 41.7 ($=CCH_3$), 70.0 (CH_2O), 74.3 (NCHPh), 100.7 (OCN), 126.1, 127.9, 128.8, 139.1, 217.6 (cis CO), 223.1 (trans CO), 278.1 (Cr=C); IR (film) ν 2052, 1906 cm^{-1}. Anal. Calcd for $C_{18}H_{17}NO_6Cr$: C, 54.68; H, 4.33; N, 3.54. Found: C, 54.43; H, 4.52; N, 3.55. This reaction also afforded 22% of the "open chain" carbene complex identical in all respects with that synthesized by the reaction of phenylglycinol with the (acetoxy)methylcarbene complex.

Pentacarbonyl[(*N*-tritylamino)(methyl)carbene]chromium(0). The tetramethyl ammonium ate complex (500 mg, 1.62 mmol) was dissolved in dry dichloromethane (10 mL), and the solution was deoxygenated and kept under argon. Acetyl bromide (120 μL, 1.62 mmol) was added at −40 °C, and the red solution was stirred for 1 h. A solution of tritylamine (630 mg, 2.4 mmol) in dichloromethane (2 mL) was added dropwise. The solution was stirred for 20 h, while the temperature was raised from −40 °C to −5 °C. Neutral alumina was added to the resulting yellow solution. Filtration through Celite, followed by purification by column chromatography/silica gel (hexane/ethyl acetate/5% triethylamine), afforded the aminocarbene as yellow crystals (800 mg, 100%). Recrystallization in ethyl acetate/hexane gave analytically pure product (86% recovery): ^1H NMR (270 MHz, $CDCl_3$) δ 2.27 (s, 3 H, $=CCH_3$), 7.14–7.44 (m, 15 H, ArH), 10.10 (br s, 1 H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.2 ($=CCH_3$), 79.3 (CPh_3), 127.9, 128.1, 128.4, 128.8, 142.6, 217.8 (cis CO), 222.6 (trans CO), 289.7 (Cr=C). Anal. Calcd for $C_{26}H_{19}NO_5Cr$: C, 65.41; H, 4.01; N, 2.93. Found: C, 65.63; H, 4.15; N, 2.97.

General Procedure for the Photolysis of Chromium Aminocarbene Complexes in Alcohol. The chromium carbene complex (0.5–0.7 mmol) was added as a solid to an oven-dried Pyrex pressure tube (Ace Glass), followed by dry alcohol (methanol or *tert*-butyl alcohol). The contents were degassed by three freeze–thaw–evacuate cycles, purged with argon, warmed to room temperature, and a pressure head attached. The system was purged with CO, pressurized with 50–90 psi CO, and irradiated with a 450 W Conrad Hanovia medium pressure UV lamp until the carbene was consumed (TLC, CH_2Cl_2/hexane, 1:1). The reaction mixture was filtered through Celite to remove solid $Cr(CO)_6$ (50–70% recovery) and other chromium residues. The solvent was removed under reduced pressure with a rotatory evaporator (when necessary at −5 °C). The resulting crude material was generally a single, pure product. When chromium residues were still observed by IR, the product could be purified by air oxidation (in a 1:1 ether/hexane or 1:3 ethylacetate/hexane solution, placed in a light box, equipped with six 20W Vitalite fluorescent lamps for 15 h), followed by filtration through Celite on a bed of silica gel and removal of the solvent. When necessary, further purification was

carried out by isolating the product as the HCl salt or by chromatography (column or radial) on silica gel.

2-(*N*,*N*-Dibenzylamino)propionic Acid *tert*-Butyl Ester (2a). From 155 mg (0.37 mmol) of **1a** was obtained the amino ester **2a** as a colorless oil (107 mg, 89%). From 75 mg (0.18 mmol) of **1a** was obtained the amino ester **2a** as a colorless oil (51 mg, 87%) when under an argon atmosphere rather than pressurized under CO: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.26 (d, J = 7.1 Hz, 3 H, CH_3), 1.52 (s, 9 H, $(CH_3)_3$), 3.37 (q, J = 7.1 Hz, 1 H, CH), 3.64 (d, J = 14.0 Hz, 2 H, CH_2), 3.84 (d, J = 14.0 Hz, 2 H, CH_2), 7.31 (m, 10 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0 (CH_3), 28.4 (CH_3), 54.4 (CH_2), 56.7 (CH), 80.7 (C), 126.8, 128.2, 128.6, 140.1, 173.1 (C=O); IR (film) ν 1724 cm^{-1}. Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.66; H, 8.29; N, 4.34.

2-*N*-Isoindolinepropionic Acid Methyl Ester (2b). Photolysis (for 7 days) of 0.17 g (0.50 mmol) of **1b** in 25 mL of methanol/THF (4:1) gave 86 mg (84%) of **2b** as a dark brown oil after air oxidation to remove residual chromium. Although colored, this material was analytically pure: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.47 (d, J = 7.0 Hz, 3 H, CH_3), 3.60 (q, J = 7.0 Hz, 1 H, NCH), 3.74 (s, 3 H, OCH_3), 4.10 (s, 4 H, NCH_2), 7.19 (s, 4 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.0 (CH_3), 51.6 (OCH_3), 55.7 (NCH_2), 60.4 (NCH), 122.2, 126.7, 139.3, 174.0 (C=O); IR (film) ν 1730 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.43; H, 7.17; N, 6.78.

2-Morpholinopropionic Acid Methyl Ester (2c). The photolysis (for 27 h) of 0.20 g (0.7 mmol) of **1c** in 10 mL of methanol gave 113 mg (100%) of **2c** as a pale yellow oil: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.31 (d, J = 7.0 Hz, 3 H, CH_3), 2.60 (t, J = 4.7 Hz, NCH_2), 3.25 (q, J = 7.0 Hz, CH), 3.70 (m, 4 H, OCH_2), 3.71 (s, 3 H, OCH_3); ^{13}C NMR (67 MHz, $CDCl_3$) δ 15.0 (CH_3), 49.8 (NCH_2), 51.0 (OCH_3), 53.1 (NCH_2), 62.7 (NCH), 65.5 (OCH_2), 67.0 (OCH_2), 172.8 (C=O). The HCl salt (43 mg, 47%), obtained by bubbling HCl gas through an ether solution, was utilized to obtain elemental analysis: mp (HCl salt) 171–172.5 °C; IR (film, HCl salt) ν 1750 cm^{-1}. Anal. Calcd for $C_8H_{16}ClNO_3$: C, 45.83; H, 7.69; N, 6.68. Found: C, 45.99; H, 7.44; N, 6.77.

2-(*N*,*N*-Dimethylamino)-2-cyclopropylacetic Acid Methyl Ester, Hydrochloride Salt (2d). Photolysis (for 17 h) of 0.20 g (0.7 mmol) of **1d** in 10 mL of methanol gave a crude reaction mixture which was filtered through Celite, taken up in water, extracted with ether, dried over Na_2SO_4, and air oxidized overnight. The resulting solution was refiltered, and HCl gas bubbled through to obtain 114 mg (85%) of **2d** as a clear oil that solidified upon standing: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.66 (m, 1 H, CH), 0.90 (m, 2 H, CH_2), 1.19 (m, 1 H, CH_2), 1.25 (m, 1 H, CH_2), 2.14 (s, 1 H, NH), 2.91 (s, 3 H, NCH_3), 3.09 (s, 3 H, NCH_3), 3.37 (d, J = 7.8 Hz, 1 H, NCH), 3.86 (s, 3 H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.2 (CH_2), 5.5 (CH_2), 10.0 (*C*H), 38.5 (NCH_3), 42.6 (NCH_3), 53.2 (OCH_3), 70.0 (NCH), 167.5 (C=O); IR (film) ν 1746 cm^{-1}. Anal. Calcd for $C_8H_{16}ClNO_2$: C, 49.61; H, 8.33; N, 7.23. Found: C, 49.44; H, 8.21; N, 7.13.

2-(*N*,*N*-Dimethylamino)-3-(benzyloxy)propionic Acid Methyl Ester (2e). Photolysis (for 2 days) of 0.23 g (0.6 mmol) of **1e** in 30 mL of methanol gave 0.12 g (82%) of **2e** as a clear to pale yellow oil after air oxidation in ether overnight: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.35 (s, 6 H, NCH_3), 3.44 (t, J = 6.5 Hz, 1 H, NCH), 3.70 (s, 3 H, OCH_3), 3.70 (m, 2 H, OCH_2), 4.53 (s, 2 H, $PhCH_2$), 7.30 (s, 5 H, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 42.2 (NCH_3), 51.0 (OCH_3), 67.2 (NCH), 68.4 (OCH_2), 73.2 (CH_2Ph), 127.5, 128.2, 137.9, 171.0 (C=O); IR (film) ν 1732 cm^{-1}. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 66.00; H, 7.82; N, 5.76.

1-(Phenylmethyl)-2-azetidinecarboxylic Acid Methyl Ester (2f). Photolysis (for 8 days) of 0.30 g (0.9 mmol) of **1f** in 16 mL of methanol gave a mixture of primarily two compounds. After column chromatography on silica gel, elution with 5% methanol/CH_2Cl_2 resulted in obtaining 82 mg (45%) of **2f** identical in all respects with material synthesized by an alternate procedure[28] and 39 mg (25%) of the acetal **2f'**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83 (q, J = 6.4 Hz, 2 H, CH_2), 2.71 (t, J = 6.9 Hz, 2 H, NCH_2), 3.32 (s, 6 H, OCH_3), 3.79 (s, 2 H, NCH_2Ph), 4.47 (t, J = 5.5 Hz, 1 H, NCH), 7.28 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.7 (CH_2), 44.9 (NCH_2), 52.9 (OCH_3), 54.0 (NCH_2Ph), 103.6 (NCHO), 126.9, 128.1, 128.4, 140.1; IR (film) ν 2823, 1453, 1126, 1066 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 67.83; H, 8.89; N, 6.69.

***N*-Methylpipecolic Acid Methyl Ester (2i).** Photolysis (for 2 days) of 0.40 g (1.4 mmol) of **1i** in 20 mL of methanol gave 195 mg (90%) of **2i** as a colorless oil.[29]

***N*-Benzylpipecolic Acid Methyl Ester (2j).** Photolysis (for 6 days) of 0.20 g (0.6 mmol) of **1j** in 7 mL of methanol gave 115 mg (90%) of **2j** as a clear liquid: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.36 (m, 1 H, CH_2), 1.57 (m, 3 H, CH_2), 1.82 (m, 3 H, CH_2), 2.15 (m, 1 H, NCH_2CH_2), 2.94 (dt, J = 11.8, 5.3 Hz, 1 H, NCH_2CH_2), 3.16 (dd, J = 4.5, 7.7 Hz, 1 H, NCH), 3.40 (d, J = 13.3 Hz, 1 H, NCH_2Ph), 3.74 (s, 3 H, OCH_3), 3.78 (d, J = 13.3 Hz, 1 H, NCH_2Ph), 7.30 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.4 (CH_2), 25.2 (CH_2), 29.5 (CH_2), 50.1 (NCH_2), 51.4 (OCH_3), 60.6 (NCH_2Ph), 64.3 (NCH), 126.9, 128.1, 129.1, 138.1, 174.3 (C=O); IR (film) ν 1738 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.04; H, 8.24; N, 6.12.

***N*-Benzyl-2-carbomethoxyazacycloheptane (2k).** Photolysis (for 2 days) of 0.20 g (0.5 mmol) of **1k** in 10 mL of methanol gave 76 mg (58%) after chromatography on silica gel (5% methanol/CH_2Cl_2): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.35 (m, 1 H, CH_2), 1.49 (m, 2 H, CH_2), 1.71 (m, 5 H, CH_2), 2.05 (m, 1 H, NCH_2CH_2), 2.66 (dt, J = 4.4, 15.5 Hz, 1 H, NCH_2), 3.08 (m, 1 H, NCH_2), 3.50 (dd, J = 5.9, 9.3 Hz, 1 H, NCH), 3.68 (s, 3 H, OCH_3), 3.79 (s, 2 H, NCH_2Ph), 7.18–7.38 (m, 5 H, ArH); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 25.3 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 31.8 (CH_2), 49.6 (NCH_2), 51.1 (OCH_3), 60.0 (NCH_2Ph), 65.0 (NCH), 126.9, 128.1, 128.7, 140.2, 175.5 (C=O); IR (film) ν 1737 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 73.00; H, 8.49; N, 5.46.

***N*-Benzyl-2-carbomethoxyazacyclotridecane (2l).** Photolysis (for 3 days) of 0.25 g (0.5 mmol) of **1l** in 4.5 mL of methanol/THF (2:1) gave 172 mg (96%) of **2l** as a clear oil: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.30 (m, 20 H, CH_2), 1.55 (m, 2 H, CH_2), 2.59 (m, 2 H, NCH_2), 3.33 (dd, J = 3.4, 10.5 Hz, 1 H, NCH), 3.46 (d, J = 13.8 Hz, 1 H, NCH_2Ph), 3.70 (s, 3 H, OCH_3), 3.96 (d, J = 13.9 Hz, 1 H, NCH_2Ph), 7.35 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 23.6 (CH_2), 25.2 (CH_2), 25.5 (CH_2), 26.3 (CH_2), 26.7 (CH_2), 27.1 (CH_2), 29.1 (CH_2), 49.9 (NCH_2), 50.8 (OCH_3), 55.2 (NCH_2Ph), 61.2 (NCH), 126.8, 128.0, 129.1, 140.3, 174.0 (C=O); IR (film) ν 1735 cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO_2$: C, 76.09; H, 10.03; N, 4.22. Found: C, 75.86; H, 9.88; N, 4.21.

2-(*N*,*N*-Diethylamino)-2-phenylacetic Acid Methyl Ester (2m). Photolysis (for 5 days) of 0.20 g (0.6 mmol) of **1m** in 10 mL of methanol gave 126 mg (100%) of **2m** as a pale yellow oil after air oxidation: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.99 (t, J = 7.1 Hz, 6 H, CH_2CH_3), 2.61 (q, J = 7.1 Hz, 4 H, NCH_2), 3.70 (s, 3 H, OCH_3), 4.49 (s, 1 H, NCH), 7.30–7.45 (m, 5 H, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 12.1 (CH_3), 43.8 (NCH_2), 51.3 (OCH_3), 69.2 (NCH), 127.7, 128.2, 128.6, 137.3, 172.7 (C=O); IR (film) ν 1740 cm^{-1}. Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.68; H, 8.51; N, 6.36.

2-(*N*,*N*-Dimethylamino)-2-(*p*-(trifluoromethyl)phenyl)acetic Acid Methyl Ester (2n). Photolysis (for 19 h) of 0.20 g (0.5 mmol) of **1n** in 10 mL of methanol gave 117 mg (88%) of **2n** as a clear liquid: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.26 (s, 6 H, NCH_3), 3.71 (s, 3 H, OCH_3), 3.96 (s, 1 H, NCH), 7.60 (m, 4 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.3 (NCH_3), 52.1 (OCH_3), 72.0 (NCH), 125.4, 127.8 (d, CF_3), 129.0, 130.6 (q, CCF_3), 140.4, 171.4 (C=O); IR (film) ν 1745 cm^{-1}. The HCl salt was obtained for elemental analysis due to the instability of the liquid. Anal. Calcd for $C_{12}H_{15}ClF_3NO_2$: C, 48.41; H. 5.07; N, 4.71. Found: C, 48.57; H, 4.93; N, 4.98.

2-(*N*,*N*-Dimethylamino)-2-(3'-furyl)acetic Acid Methyl Ester, Hydrochloride (2o). Photolysis (for 21 h) of 0.40 g (1.3 mmol) of **1o** in 20 mL of methanol gave 298 mg of **2o** as a pale orange residue. This residue was taken up in methanol/water extracted with ether (6×), dried over $CaCl_2$, and filtered through Celite, and HCl gas was bubbled through to get a white precipitate. Recrystallization from MeOH/Et_2O gave 221 mg of the HCl salt as white crystals (76% yield) for elemental analysis: mp 152–153 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.87 (s, 6 H, NCH_3), 3.87 (s, 3 H, OCH_3), 5.07 (s, 1 H, NCH), 6.73 (d, J = 1.5 Hz, 1 H, 4-furyl CH), 7.51 (s, 1 H, 5-furyl CH), 7.81 (s, 1 H, 2-furyl CH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 40.6 (NCH_3), 53.3 (OCH_3), 61.5 (NCH), 110.4 (4'-furyl), 113.5 (3'-furyl), 144.4 (5'-furyl), 145.0 (2'-furyl), 166.6 (C=O); IR (film, HCl salt) ν 1748 cm^{-1}. Anal. Calcd for $C_9H_{14}ClNO_3$: C, 49.21; H, 6.42; N, 6.38. Found: C, 49.22; H, 6.69; N, 6.39.

Photolysis (for 4 days) of 0.06 g (0.5 mmol) of **1q** resulted in total consumption of the carbene and gave a pale orange residue, which consisted primarily of cinnamaldehyde (by ^{1}H NMR spectroscopy).

2-(1-Aza-3-oxa-5(*S*)-phenylcyclopentyl)propionic Acid Methyl Ester (4a). Photolysis (for 2 days) of 0.16 g (0.4 mmol) of **3a** in 15 mL of methanol gave 86 mg (86%) of **4a** as a clear oil after chromatography on alumina (hexane/EtOAc, 2:1). This was a mixture of two diastereoisomers noted in the ^{1}H NMR spectrum as a 86:14 ratio by the pair of methyl doublets: ^{1}H NMR (200 MHz, $CDCl_3$) δ (major diastereoisomer) 1.27 (d, J = 7.3 Hz, 3 H, CH_3), 3.52 (q, J = 7.3 Hz, 1 H, $NCHCH_3$), 3.61 (m, 1 H, NCHPh), 3.68 (s, 3 H, OCH_3), 4.25 (m, 2 H, CH_2O), 4.72 (s, 2 H, NCH_2O), 7.34 (m, 5 H, ArH); δ (minor diastereoisomer) 1.27 (d, J = 6.2 Hz, 3 H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (major diastereoisomer) 17.3 (CH_3), 51.4 (OCH_3), 56.3 (OCH_2), 64.0 (NCHPh), 74.3 (NCH), 82.6 (NCH_2O), 127.2, 127.5, 128.5, 140.3, 173.3 (C=O); IR (film) ν 1740 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.62; H, 7.53; N, 5.66.

2-(1-Aza-2-*trans*-isopropyl-3-oxa-5(*S*)-phenylcyclopentyl)propionic Acid Methyl Ester (4b). Photolysis (for 18 h) of 0.10 g (0.2 mmol) of **3b** in 8.5 mL of methanol gave 67 mg (100%) of **4b** as a clear liquid. This was a mixture of two diastereoisomers noted in the ^{1}H NMR spectrum as a 87:13 ratio by the pair of methyl doublet of doublets: ^{1}H NMR (270 MHz, $CDCl_3$) δ (major diastereoisomer) 1.02 (d, J = 6.5 Hz, 3 H, CH_3), 1.04 (d, J = 6.5 Hz, 3 H, CH_3), 1.31 (d, J = 7.2 Hz, 3 H, NCHCH_3), 1.82 (m, 1 H, CH(CH_3)$_2$), 3.54 (s, 3 H, OCH_3), 3.63 (m, 1 H, NCHCH$_3$), 4.19 (t, J = 7.7 Hz, 1 H, OCH_2), 4.38 (t, J = 7.7 Hz, 1 H, NCHPh), 4.48 (d, J = 4.7 Hz, 1 H, OCH_2), 7.31, 7.42 (m, 5 H, ArH); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ (major diastereoisomer) 15.1 (CH_3), 16.1 (CH_3), 19.0 (CH_3), 32.9 (CH), 51.2 (OCH_3), 56.8 (OCH_2), 64.4 (NCHPh), 73.3 (NCH), 98.0 (NCHO), 126.9, 127.2, 127.3, 128.3, 141.0, 173.1 (C=O); IR (film) ν 1742 cm^{-1}. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.28; H, 8.36; N, 5.05. Found: C, 69.00; H, 8.30; N, 5.20.

2-(1-Aza-2-*trans*-isopropyl-3-oxa-5(*S*)-phenylcyclopentyl)propionic Acid *tert*-Butyl Ester (4b′). From 129 mg (0.31 mmol) of **3b** was obtained the amino ester **4b′** as a colorless oil (82 mg; 81%; 42% de): ^{1}H NMR (270 MHz, $CDCl_3$) δ (major diastereoisomer) 1.01 (d, J = 6.8 Hz, 3 H, CH_3), 1.04 (d, J = 6.9 Hz, 3 H, CH_3), 1.26 (d, J = 7.2 Hz, 3 H, CH_3), 1.39 (s, 9 H, $(CH_3)_3$), 1.82 (m, 1 H, CH), 3.43 (q, J = 7.2 Hz, 1 H, CH), 3.64 (t, J = 8.0 Hz, 1 H, CH), 4.18 (t, J = 7.7 Hz, 1 H, CH), 4.43 (t, J = 7.7 Hz, 1 H, CH), 4.53 (d, J = 8.1 Hz, 1 H, CH), 7.28, 7.42 (m, 5 H, ArH); δ (minor diastereoisomer) 1.02 (d, J = 6.7 Hz, 3 H, CH_3), 1.06 (d, J = 7.7 Hz, 3 H, CH_3), 1.09 (d, J = 7.7 Hz, 3 H, CH_3), 1.84 (m, 1 H, CH), 1.49 (s, 9 H, $(CH_3)_3$), 3.52 (q, J = 7.2 Hz, 1 H, CH), 3.71 (dd, J = 8.0, 5.6 Hz, 1 H, CH), 4.25 (t, J = 7.8 Hz, 1 H, CH), 4.41 (d, J = 7.8 Hz, 1 H, CH), 4.58 (dd, J = 5.9, 7.1 Hz, 1 H, CH), 7.25, 7.42 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereoisomer) 16.1 (CH_3), 16.2 (CH_3), 19.1 (CH_3), 28.0 (CH_3), 33.0 (CH), 57.6 (OCH_2), 64.7 (NCHPh), 73.2 (NCH), 80.8 (C), 97.7 (NCHO), 126.8, 127.2, 128.3, 141.3, 172.1 (C=O); δ (minor diastereoisomer) 16.5 (CH_3), 17.1 (CH_3), 18.8 (CH_3), 28.2 (CH_3), 31.7 (CH), 61.8 (NCHPh), 74.0 (NCH), 81.0 (C), 99.0 (NCHO), 126.9, 128.1, 144.8, 173.1 (C=O); IR (film) ν 1726 cm^{-1}. Anal. Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.52; H, 8.97; N, 4.44.

2-(1-Aza-2-dimethyl-3-oxa-5(*S*)-phenylcyclopentyl)propionic Acid Methyl Ester (4c). Photolysis (for 24 h) of 0.14 g (0.4 mmol) of **3c** in 8 mL of methanol gave 91 mg (100%) of a single diastereoisomer **4c** as a clear liquid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.27 (d, J = 7.0 Hz, 3 H, CHCH_3), 1.34 (s, 3 H, CCH_3), 1.51 (s, 3 H, CCH_3), 3.45 (s, 3 H, CH_3), 3.57 (q, J = 7.0 Hz, 1 H, NCH), 3.66 (t, J = 7.7 Hz, 1 H, OCH_2), 4.18 (t, J = 7.7 Hz, 1 H, OCH_2), 4.45 (t, J = 7.2 Hz, 1 H, NCHPh), 7.31 (m, 5 H, ArH); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 15.3 (CH_3), 23.1 (CH_3), 28.8 (CH_3), 51.3 (OCH_3), 53.2 (NCHPh), 62.1 (OCH_2), 72.2 (NCH), 96.0 (NCO), 127.4, 127.6, 128.3, 141.8, 174.3 (C=O); IR (film) ν 1740 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.30; H, 7.81; N, 5.34.

2-(1-Aza-2-dimethyl-3-oxa-5(*S*)-phenylcyclopentyl)propionic Acid *tert*-Butyl Ester (4c′). From 130 mg (0.33 mmol) of complex **3c** was obtained the amino ester **4c′** as a colorless oil (69 mg; 68%; ≥88% de). From 133 mg (0.33 mmol) of **3c** was obtained the amino ester **4c′** as a colorless oil (79 mg; 77%; ≥93% de, when under an argon atmosphere rather than pressurized under CO): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.21 (d, J = 7.1 Hz, 3 H, CH_3), 1.35 (s, 12 H, CH_3), 1.51 (s, 3 H, CH_3), 3.46 (q, J = 7.1 Hz, 1 H, CH), 3.63 (m, 1 H, OCH_2), 4.16 (dd, J = 7.1, 7.2 Hz, 1 H, OCH_2), 4.47 (t, J = 7.2 Hz, 1 H, NCHPh), 7.30 (m, 5 H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8 (CH_3), 22.9 (CH_3), 27.8 (CH_3), 29.0 (CH_3), 54.4 (NCHPh), 62.4 (OCH_2), 72.1 (NCH), 80.3 (C), 96.0 (NCO), 127.2, 127.5, 128.3, 142.1, 173.3 (C=O); IR (film) ν 1726 cm^{-1}. Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.78; H, 8.91; N, 4.58. Found: C, 70.70; H, 9.01; N, 4.63.

Pentacarbonyl[(*N*-benzylamino)(methyl)carbene]chromium(0) (8). Pentacarbonyl[(methoxy)(methyl)carbene]chromium(0) (5.5 g, 22 mmol) was dissolved in deoxygenated methanol (100 mL). Benzylamine (2.5 mL, 23 mmol) was added under argon. After 15 min, the yellow solution was cooled to 0 °C, and a first crop of crystals was collected by filtration. The filtrate was concentrated, and the residue was recrystallized from ether–hexane to give a total of 6.3 g (88%) of aminocarbene **8**.[32]

Pentacarbonyl[(*N*,*N*-dibenzylamino)(methyl)carbene]chromium(0) (1a). The aminocarbene complex **8** (3.25 g, 10 mmol) was dissolved in dry deoxygenated dimethylformamide (50 mL) and added at 0 °C under argon to sodium hydride (393 mg, 60% suspension in oil, 9.5 mmol, washed with dry hexane). The yellow solution was stirred for 20 min and then benzyl bromide (1.16 ml, 9.8 mmol) was added. Stirring was continued for 15 h at 0 °C, and then the solution was treated with aqueous ammonium chloride (50 mL). The aminocarbene complex **1a** was extracted with ether–hexane (2 × 50 mL), and the combined organic layers were dried over magnesium sulfate and filtered. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (elution with 10% of ether in hexane) to give 3.37 g (81% based on 8) of aminocarbene **1a**[12] and 0.24 g (7%) of recovered **4**.

General Procedures for the Synthesis of α-Amino Esters from Chromium Aminocarbene Complexes. Method A: Deprotonation with Butyllithium in THF. The aminocarbene (0.40 mmol) was dissolved in dry THF (2 mL). The solution was cooled to −78 °C, deoxygenated in vacuo (three cycles), and kept under argon. Butyllithium (0.44 mmol; 2 M in hexane) was added at −30 °C. After 15 min, the alkyl halide (0.44 mmol) was added, the cooling bath was removed, and stirring was continued for the time indicated below. The reaction mixture was diluted with wet ether (5 mL), treated with magnesium sulfate, and filtered directly through a short bed of silica gel (elution with ether). The yellow filtrate was concentrated in vacuo to give the alkylated aminocarbene that could be isolated and characterized, if desired. More practically, the residue was taken in dry alcohol (methanol, ethanol, or *tert*-butyl alcohol) and transferred into a pressure vessel, and the solution was rapidly deoxygenated by bubbling argon through for 5 min. Irradiation was performed as described above under 75 psi of carbon monoxide for 15–24 h. Chromium hexacarbonyl was removed by filtration, and the yellow filtrate was concentrated in vacuo. The residue was dissolved in ether–hexane (8 mL) and photooxidized in a lightbox for several hours. Filtration of the precipitate through a short bed of silica gel (elution with ether) and evaporation of the solvent afforded the amino ester that was further purified by radial chromatography on silica gel by using a gradient of ether in hexane.

Method B: Deprotonation with Sodium Hydride in DMF. Sodium hydride (0.37 mmol; 60% suspension in oil) was washed with hexane and dried in vacuo. The flask was cooled to 0 °C under argon, and a solution of the amino carbene (0.33 mmol) in DMF (2 mL) was added with a syringe. The solution was vented several times under vacuum and placed under an argon atmosphere. After 10 min at 0 °C, the alkyl halide (0.34 mmol) was added, and stirring was continued at the temperature and for the time indicated below. A saturated solution of ammonium chloride (5 mL) was added, and the aminocarbene was extracted into ether–hexane (1:1) several times. The combined organic layers were dried over magnesium sulfate and filtered through a short bed of silica gel (elution with ether). The yellow filtrate was concentrated, and the residue was submitted to the photolytic conditions as described above.

Method C: Deprotonation with Bis(trimethylsilyl)amide in THF/Toluene. The aminocarbene complex (0.43 mmol) was dissolved in dry THF (1.5 mL), and the solution was cooled to −78 °C. After deoxygenation in vacuo, 940 μL (0.47 mmol) of potassium bistrimethylsilyl amide (0.5 M solution in hexane) was added dropwise under argon at −60 °C. After 10 min, the clear orange solution was treated with the alkyl halide (0.47 mmol), and the solution was allowed to slowly warm to room temperature during the time indicated below. Addition of wet ether, drying over magnesium sulfate, and filtration through a short bed of silica gel (elution with ether) were followed by photolysis in methanol as described in method A.

2-(*N*,*N*-Dibenzylamino)-5-hexenoic Acid Methyl Ester (11a). According to method A, 122 mg (0.29 mmol) of **1a** was alkylated for 1 h with 161 μL (0.32 mmol) of butyllithium and 28 μL (0.40 mmol) of allyl bromide. Photolysis in methanol afforded **11a** (68 mg; 72%) as a clear colorless oil after purification by radial chromatography. Carbene: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.32 (m, 2 H, CH_2), 3.37 (m, 2 H, CH_2), 4.68 (s, 2 H, NCH_2), 5.04 (dd, J = 1.0 and 10.1 Hz, 1 H, CH_2=), 5.11 (dd, J = 1.0 and 17.0 Hz, 1 H, CH_2=), 5.39 (s, 2 H, NCH_2), 5.82 (m, 1 H, CH=), 7.00–7.45 (m, 10 H, Ar).

11a: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.82 (m, 2 H, CH_2), 1.98 (m, 1 H, CH_2), 2.19 (m, 1 H, CH_2), 3.34 (t, J = 7.5 Hz, 1 H, CH), 3.52 (d, J = 13.8 Hz, NCH_2), 3.75 (s, 3 H, OCH_3), 3.92 (d, J = 13.6 Hz, NCH_2), 4.87 (m, 2 H, CH_2=), 5.66 (m, 1 H, CH=), 7.35 (m, 10 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.0 (CH_2), 30.3 (CH_2), 51.0 (OCH_3), 54.6 (NCH_2), 60.4 (CHN), 114.9 (=CH_2), 127.0, 128.2, 128.9, 137.8 (=CH), 139.6, 173.4 (C=O); IR (film) ν 1732 cm^{-1}. Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.97; H, 7.63; N, 4.21.

2-(*N*,*N*-Dibenzylamino)-4-phenylbutanoic Acid Methyl Ester (11b). According to method A, 154 mg (0.37 mmol) of **1a** was alkylated for 1 h with 204 μL (0.40 mmol) of butyllithium and 48 μL (0.40 mmol) of benzyl bromide. Photolysis in methanol afforded **11b** (99 mg; 72%) as a clear colorless oil after purification by radial chromatography. Carbene: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.87 (m, 2 H, CH_2), 3.57 (m, 2 H, CH_2), 4.77 (s, 2 H, NCH_2), 5.43 (s, 2 H, NCH_2), 7.00–7.45 (m, 15 H, Ar).

11b: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.03 (q, J = 7.7 Hz, 2 H, CH_2), 2.47 (dt, J = 13.9 and 8 Hz, 1 H, CH_2), 2.77 (m, 1 H, CH_2), 3.39 (t, J = 7.4 Hz, 1 H, CH), 3.55 (d, J = 13.8 Hz, 2 H, NCH_2), 3.74 (s, 3

H, OCH_3), 3.95 (d, J = 13.8 Hz, 2 H, NCH_2), 7.20 (m, 10 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.6 (CH_2), 32.5 (CH_2), 51.0 (OCH_3), 54.7 (NCH_2), 60.6 (CHN), 125.8, 127.0, 128.3, 128.4, 128.6, 128.9, 139.6, 141.7, 173.3 (C=O); IR (film) ν 1731 cm^{-1}. Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.39; H, 7.29; N, 3.75. Found: C, 80.50; H, 7.19; N, 3.59.

2-(*N*,*N*-Dibenzylamino)-4-(4'-methoxyphenyl)butanoic Acid Methyl Ester (11c). According to method A, 159 mg (0.38 mmol) of **1a** was alkylated for 4 h with 200 μL (0.40 mmol) of butyllithium and 53 μL (0.39 mmol) of 4-methoxybenzyl chloride. Photolysis in methanol afforded **11c** (112 mg; 73%) as a clear colorless oil after purification by radial chromatography. Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 2.82 (m, 2 H, CH_2), 3.54 (m, 2 H, CH_2), 3.76 (s, 3 H, OCH_3), 4.76 (s, 2 H, NCH_2), 5.42 (s, 2 H, NCH_2), 7.00–7.45 (m, 14 H, Ar).

11c: ^1H NMR (270 MHz, $CDCl_3$) δ 1.99 (q, J = 7.6 Hz, 2 H, CH_2), 2.42 (m, 1 H, CH_2), 2.70 (m, 1 H, CH_2), 3.37 (t, J = 7.3 Hz, 1 H, CHN), 3.55 (d, J = 13.8 Hz, 2 H, NCH_2), 3.74 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 3.94 (d, J = 13.8 Hz, 2 H, NCH_2), 6.73 (d, J = 8.9 Hz, 2 H, Ar), 6.92 (d, J = 8.9 Hz, 2 H, Ar), 7.31 (m, 10 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.5 (CH_2), 31.8 (CH_2), 51.0 (OCH_3), 54.7 (NCH_2), 55.2 (OCH_3), 60.5 (CHN), 113.8, 127.0, 128.2, 128.9, 129.2, 133.8, 139.6, 157.8, 173.3 (C=O); IR (film) ν 1731 cm^{-1}. Anal. Calcd for $C_{26}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47. Found: C, 77.19; H, 7.30; N, 3.29.

***N*,*N*-Dibenzylglutamic Acid Diethyl Ester (11d).** According to method **B**, 137 mg (0.33 mmol) of **1a** was alkylated during 5 h with 15 mg (0.37 mmol) of sodium hydride and 38 μL (0.34 mmol) of bromoacetic acid ethyl ester. Photolysis in ethanol afforded **11d** (83 mg; 66%) as a colorless oil after purification by radial chromatography. Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 1.25 (t, J = 7.0 Hz, 3 H, CH_3), 2.60 (dd, J = 8.1 and 8.5 Hz, 2 H, CH_2), 3.55 (dd, J = 8.1 and 8.5 Hz, 2 H, CH_2), 4.14 (q, J = 7.0 Hz, 2 H, OCH_2), 4.74 (s, 2 H, NCH_2), 5.42 (s, 2 H, NCH_2), 7.21 (m, 10 H, Ar).

11d: ^1H NMR (270 MHz, $CDCl_3$) δ, 1.19 (t, J = 7.2 Hz, 3 H, CH_3), 1.35 (t, J = 7.1 Hz, 3 H, CH_3), 2.03 (m, 2 H, CH_2), 2.39 (m, 2 H, CH_2), 3.33 (t, J = 7.6 Hz, CHN), 3.53 (d, J = 13.7 Hz, 2 H, NCH_2), 3.91 (d, J = 13.7 Hz, 2 H, NCH_2), 4.00 (m, 2 H, OCH_2), 4.20 (m, 2 H, OCH_2), 7.33 (m, 10 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1 (CH_3), 14.6 (CH_3), 24.3 (CH_2), 30.7 (CH_2), 54.5 (NCH_2), 59.7 (OCH_2), 60.2 (OCH_2), 60.3 (CHN), 127.0, 128.3, 128.9, 139.3, 172.3 (C=O), 173.0 (C=O); IR (film) ν 1732 cm^{-1}. Anal. Calcd for $C_{23}H_{29}NO_4$: C, 72.03; H, 7.62; N, 3.65. Found: C, 71.80; H, 7.50; N, 3.49.

2-(*N*,*N*-Dibenzylamino)heptanoic Acid Methyl Ester (11e). According to method **B**, 178 mg (0.42 mmol) of **1a** was alkylated for 15 h with 20 mg (0.50 mmol) of sodium hydride and 51 μL (0.45 mmol) of butyl iodide. Photolysis in methanol afforded **11e** (68 mg; 48%) as a colorless oil after purification by radial chromatography. Carbene: ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, J = 6.9 Hz, 3 H, CH_3), 1.25–1.57 (m, 6 H, CH_2), 3.25 (m, 2 H, CH_2), 4.65 (s, 2 H, NCH_2), 5.37 (s, 2 H, NCH_2), 7.00–7.45 (m, 10 H, Ar).

11e: ^1H NMR (270 MHz, $CDCl_3$) δ 0.84 (t, J = 7.2 Hz, 3 H, CH_3), 1.24 (m, 6 H, CH_2), 1.70 (m, 2 H, CH_2), 3.32 (t, J = 7.3 Hz, 1 H, CHN), 3.51 (d, J = 14 Hz, 2 H, NCH_2), 3.76 (s, 3 H, OCH_3), 3.94 (d, J = 14 Hz, 2 H, NCH_2), 7.32 (m, 10 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0 (CH_3), 22.5 (CH_2), 25.7 (CH_2), 29.5 (CH_2), 31.4 (CH_2), 50.9 (OCH_3), 54.5 (NCH_2), 60.7 (CHN), 126.9, 128.2, 128.8, 139.8, 173.7 (C=O); IR (film) ν 1733 cm^{-1}. Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 78.00; H, 8.39; N, 4.07.

2-*N*-Isoindolinyl-5-hexenoic Acid Methyl Ester (12a). According to method C, 145 mg (0.43 mmol) of **10** was alkylated during 2 h with 940 μL (0.48 mmol) of potassium bis(trimethylsilyl)amide and 41 μL (0.47 mmol) of allyl bromide. Photolysis in methanol afforded **12a** (54 mg; 51%) as a clear colorless oil after purification by radial chromatography. This oil turned rapidly red on standing. Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 2.33 (m, 2 H, CH_2), 3.20 (m, 2 H, CH_2), 5.04 (s, 2 H, NCH_2), 5.10 (dd, J = 1.2 and 10.1 Hz, 1 H, CH_2=), 5.18 (dd, J = 1.2 and 17.0 Hz, 1 H, CH_2=), 5.46 (s, 2 H, NCH_2), 5.87 (m, 1 H, CH=), 7.39 (m, 4 H, Ar).

12a: ^1H NMR (270 MHz, $CDCl_3$) δ 1.92 (m, 2 H, CH_2), 2.18 (m, 2 H, CH_2), 3.54 (t, J = 7.2 Hz, 1 H, CHN), 3.71 (s, 3 H, OCH_3), 4.09 (d, J = 10.8 Hz, NCH_2), 4.17 (d, J = 10.8 Hz, NCH_2), 5.02 (m, 2 H, CH_2=), 5.83 (m, 1 H, CH=), 7.19 (s, 4 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1 (CH_2), 30.2 (CH_2), 51.3 (OCH_3), 55.2 (NCH_2), 63.7 (CHN), 115.3 (=CH_2), 122.3, 126.6, 137.6 (=CH), 139.4, 173.4 (C=O); IR (film) ν 1734 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.80; N, 5.71. Found: C, 73.42; H, 7.65; N, 5.75.

2-*N*-Isoindolinyl-4-(4'-methoxyphenyl)butanoic Acid Methyl Ester (12b). According to method C, 147 mg (0.44 mmol) of **10** was alkylated during 2 h with 960 μL (0.48 mmol) of potassium bis(trimethylsilyl)-amide and 65 μL (0.48 mmol) of 4-methoxybenzyl chloride. Photolysis in methanol afforded **12b** (48 mg; 33%) as a clear colorless oil after purification by radial chromatography. This oil turned red rapidly on standing. Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 2.82 (m, 2 H, CH_2), 3.36 (m, 2 H, CH_2), 3.77 (s, 3 H, OCH_3), 5.03 (s, 2 H, NCH_2), 5.48 (s, 2 H, NCH_2), 6.86 (d, J = 8.2 Hz, Ar), 7.28 (m, 6 H, Ar).

12b: ^1H NMR (270 MHz, $CDCl_3$) δ 2.10 (m, 2 H, CH_2), 2.69 (t, J = 7.7 Hz, 2 H, CH_2), 3.51 (t, J = 7.3 Hz, 1 H, CHN), 3.70 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 4.12 (d, J = 11.0 Hz, 2 H, NCH_2), 4.19 (d, J = 11.0 Hz, 2 H, NCH_2), 6.87 (d, J = 8.6 Hz, 2 H, Ar), 7.13 (d, J = 8.6 Hz, 2 H, Ar), 7.20 (s, 4 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.3 (CH_2), 32.9 (CH_2), 51.3 (OCH_3), 55.2 (NCH_2), 55.3 (OCH_3), 63.2 (CHN), 113.9, 122.3, 126.7, 129.4, 133.4, 139.4, 158.0, 173.4 (C=O). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.68; H, 6.94; N, 4.16.

3-Benzylpiperidine-2-carboxylic Acid Methyl Ester (14). According to method **B**, 113 mg (0.39 mmol) of **13** was alkylated during 3 h with 19 mg (0.46 mmol) of sodium hydride and 49 μL (0.41 mmol) of benzyl bromide. Photolysis in methanol afforded **14** (50 mg; 52%) as two syn/anti isomers (1/1 mixture) separable by radial chromatography. Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 1.38 (m, 2 H, CH_2), 1.83 (m, 1 H, CH_2), 2.11 (m, 1 H, CH_2), 2.25 (m, 1 H, CH_2Ph), 3.32 (dd, J = 3.4 and 13.8 Hz, 1 H, CH_2Ph), 3.58 (t, J = 7.1 Hz, 2 H, NCH_2), 3.80 (s, 3 H, NCH_3), 3.91 (m, 1 H, C*H*), 7.31 (m, 5 H, Ar).

14 (syn isomer): ^1H NMR (270 MHz, $CDCl_3$) δ 1.48 (m, 3 H, CH_2), 1.75 (m, 1 H, CH_2), 2.17 (m, 1 H, NCH_2), 2.32 (s, 3 H, NCH_3), 2.46 (m, 2 H, CH and CH_2Ph), 2.63 (dd, J = 6.1 and 13.6 Hz, 1 H, CH_2Ph), 2.94 (m, 1 H, NCH_2), 3.36 (d, J = 4.7 Hz, 1 H, CHN), 3.72 (s, 3 H, OCH_3), 7.22 (m, 5 H, Ar; ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2 (CH_2), 24.5 (CH_2), 38.1 (CH), 40.1 (CH_2), 43.8 (NCH_3), 50.5 (NCH_2), 50.7 (OCH_3), 67.2 (CHN), 126.0, 128.3, 129.0, 140.1, 172.2 (C=O); IR (film) ν 1728 cm^{-1}.

14 (anti isomer): ^1H NMR (270 MHz, $CDCl_3$) δ 0.87 (m, 1 H, CH_2), 1.62 (m, 3 H, CH_2), 2.02 (m, 2 H, NCH_2 and CHBn), 2.24 (s, 3 H, NCH_3), 2.31 (dd, J = 9.5 and 13.5 Hz, 1 H, CH_2Ph), 2.50 (d, J = 9.4 Hz, 1 H, CH), 2.65 (dd, J = 4.2 and 13.5 Hz, 1 H, CH_2Ph), 2.92 (m, 1 H, NCH_2), 3.74 (s, 3 H, OCH_3), 7.21 (m, 5 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.6 (CH_2), 28.4 (CH_2), 39.2 (CH), 40.6 (CH_2), 44.5 (NCH_3), 51.8 (NCH_2), 55.5 (OCH_3), 74.4 (CHN), 126.0, 128.2, 129.2, 139.4, 173.5 (C=O); IR (film) ν 1735 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.68; H, 8.38; N, 5.68.

2-(1-Aza-2,2-dimethyl-3-oxa-5(*S*)-phenylcyclopentyl)-4-phenyl-(*R*)-butanoic Acid *tert*-Butyl Ester (15a). The reaction was carried out according to method A, expect that the deprotonation was performed at −78 °C. The alkylation time was 2 h. From 198 mg (0.50 mmol) of **3c**, 212 μL (0.53 mmol) of butyllithium (2.5 M in hexane), and 65.4 μL (0.55 mmol) of benzyl bromide was obtained **15a** as a colorless oil (84 mg; 42%) after purification by radial chromatography. Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 1.78 (s, 3 H, CH_3), 1.93 (s, 3 H, CH_3), 2.69 (m, 1 H, CH_2), 3.61 (m, 3 H, CH_2), 4.20 (dd, J = 1.7 and 9.5 Hz, 1 H, OCH_2), 4.60 (dd, J = 5.6 and 9.5 Hz, 1 H, OCH_2), 5.93 (d, J = 5.6 Hz, 1 H, NCH), 7.34 (m, 10 H, Ar).

15a: ^1H NMR (270 MHz, $CDCl_3$) δ 1.27 (s, 3 H, CH_3), 1.36 (s, 9 H, CH_3), 1.50 (s, 3 H, CH_3), 1.81 (m, 1 H, CH_2), 2.21 (m, 1 H, CH_2), 2.51 (m, 2 H, CH_2), 3.26 (dd, J = 4.8 and 9.5 Hz, 1 H, CHN), 3.66 (m, 1 H, CH_2O), 4.15 (m, 1 H, CH_2O), 4.52 (t, J = 6.9 Hz, 1 H, CHN), 7.00–7.40 (m, 10 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9 (CH_3), 27.9 (CH_3), 29.1 (CH_3), 31.7 (CH_2), 33.2 (CH_2), 58.7 (OCH_2), 62.3 (CHN), 72.11 (CHN), 80.6 (C), 96.1 (C), 125.9, 127.3, 127.6, 128.2, 128.3, 128.4, 141.5, 142.2, 172.0 (C=O); IR (film) ν 1725 cm^{-1}. Anal. Calcd for $C_{25}H_{33}NO_3$: C, 75.91; H, 8.41; N, 3.54. Found: C, 76.01; H, 8.17; N, 3.65.

2-(1-Aza-2,2-dimethyl-3-oxa-5(*S*)-phenylcyclopentyl)-(*R*)-glutaric Acid α-Methyl γ-*tert*-Butyl Ester (15b). According to the above procedure, the amino ester **15b** was prepared from 195 mg (0.50 mmol) of **3c**, 209 μL (0.52 mmol) of butyllithium (2.5 M in hexane), and 87.5 μL (0.54 mmol) of bromoacetic acid *tert*-butyl ester. The product was obtained as a colorless oil (97 mg; 52%) after purification by radial chromatography: Carbene: ^1H NMR (270 MHz, $CDCl_3$) δ 1.51 (s, 9 H, CH_3), 1.83 (s, 3 H, CH3), 1.89 (s, 3 H, CH_3), 2.52 (m, 1 H, CH_2), 3.06 (m, 1 H, CH_2), 3.55 (m, 2 H, CH_2), 4.18 (dd, J = 1.5 and 9.3 Hz, 1 H, CH_2O), 4.57 (dd, J = 5.6 and 9.3 Hz, 1 H, CH_2O), 5.90 (d, J = 5.4 Hz, 1 H, CHN), 7.20–7.40 (m, 5 H, Ar).

15b: ^1H NMR (270 MHz, $CDCl_3$) δ 1.36 (s, 3 H, CH_3), 1.40 (s, 9 H, CH_3), 1.52 (s, 3 H, CH_3), 1.90 (m, 1 H, CH_2), 2.17 (m, 3 H, CH_2), 3.39 (dd, J = 5.3 and 7.9 Hz, 1 H, CHN), 3.46 (s, 3 H, OCH_3), 3.68 (dd, J = 6.9 and 7.3 Hz, 1 H, OCH_2), 4.18 (dd, J = 6.9 and 7.8 Hz, 1 H, OCH_2), 4.52 (t, J = 6.9 Hz, 1 H, CHN), 7.30 (m, 5 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2 (CH_3), 24.6 (CH_2), 28.0 (CH_3), 28.9 (CH_3), 32.3 (CH_2), 51.3 (OCH_3), 56.8 (OCH_2), 62.2 (CHN), 72.0

(CHN), 80.3 (C), 95.7 (C), 127.5, 127.6, 128.3, 141.3, 172.2 (C=O), 173.2 (C=O); IR (film) ν 1731 cm^{-1}. Anal. Calcd for $C_{21}H_{31}NO_5$: C, 66.82; H, 8.28; N, 3.71. Found: C, 66.58; H, 8.06; N, 3.55.

Acknowledgment. Support for this research under Grant 2 RO1 GM26178-10 from the National Institutes of General Medical Sciences (Public Health Service) (chemistry in Scheme I and Table I) and Grant CHE 870152 from the National Science Foundation (chemistry in Scheme II) is gratefully acknowledged. Mass spectrometry determinations were performed by Midwest Center for Mass Spectrometry, a National Science Foundation Regional Instrumentation facility (Grant No. CHE-8620177). S. De Lombaert thanks NATO for financial support.

Registry No. 1a, 117041-11-9; **1b**, 117041-12-0; **1c**, 112044-04-9; **1d**, 124716-04-7; **1e**, 112068-80-1; **1f**, 124685-61-6; **1g**, 112044-05-0; **1h**, 124685-62-7; **1i**, 124685-63-8; **1j**, 124685-64-9; **1k**, 124685-65-0; **1l**, 124685-66-1; **1m**, 117041-17-5; **1n**, 117041-14-2; **1o**, 112044-01-6; **1p**, 124685-67-2; **1q**, 124815-34-5; **1r**, 117041-19-7; **1s**, 67012-34-4; **1t**, 32370-44-8; **2a**, 124619-63-2; **2b**, 124619-64-3; **2c**, 124619-65-4; **2d**, 124619-66-5; **2e**, 124619-67-6; **2f**, 18085-37-5; **2f'**, 124619-68-7; **2i**, 1690-74-0; **2j**, 124619-69-8; **2k**, 124619-70-1; **2l**, 124619-71-2; **2m**, 105394-78-3; **2n**, 124619-72-3; **2o**, 124619-73-4; **2t**, 124619-74-5; **3a**, 124685-68-3; **3b**, 124685-69-4; **3c**, 124685-70-7; **4a** (isomer 1), 124619-75-6; **4a** (isomer 2), 124619-76-7; **4b** (isomer 1), 124619-77-8; 4b (isomer 2), 124619-78-9; **4b'** (isomer 1), 124619-79-0; **4b'** (isomer 2), 124650-74-4; **4c**, 124619-80-3; **4c'**, 124619-81-4; **7**, 20540-69-6; **8**, 12289-28-0; **11a**, 124619-82-5; **11b**, 124619-83-6; **11c**, 124619-84-7; **11d**, 124619-85-8; **11e**, 124619-86-9; **12a**, 124619-87-0; **12b**, 124619-88-1; *syn*-**14**, 124619-89-2; *anti*-**14**, 124650-75-5; **15a**, 124619-90-5; **15b**, 124619-91-6; $Na_2Cr(CO)_5$, 51233-19-3; $(CO)_5Cr{=}C(CH_3)NHCPh_3$, 124685-71-8; $K_2Cr(CO)_5$, 107799-34-8; $(CO)_5Cr{=}C(CH_3)O^-NMe_4^+$, 15975-93-6; $(CO)_5Cr{=}C(OMe)C{\equiv}CPh$, 99824-96-1; $(CO)_5Cr{=}C(OMe)C_6H_4$-*p*-CF_3, 27637-27-0; $(CO)_5Cr{=}C(OMe)Ph$, 27436-93-7; Br_2NH, 103-49-1; *N*-isoindolineacetamide, 18913-38-7; *N,N*-dibenzylacetamide, 10479-30-8; *N*-acetylmorpholine, 1696-20-4; *N,N*-dimethylcyclopropanecarboxamide, 17696-23-0; *N,N*-dimethyl-α-(phenyloxy)acetamide, 10397-59-8; *N*-benzylazetidinone, 4458-64-4; *N*-methylpyrrolidin-2-one, 872-50-4; *N*-benzylpyrrolidin-2-one, 5291-77-0; *N*-methylpiperidin-2-one, 931-20-4; *N*-benzylpiperidin-2-one, 4783-65-7; *N*-benzyl-2-azacycloheptanone, 33241-96-2; *N*-benzyl-2-azacyclotridecanone, 41011-68-1; *N,N*-diethylbenzenecarboxamide, 1696-17-9; *N,N*-dimethyl-3-furancarboxamide, 14757-80-3; 2-chloro-*N,N*-dimethylbenzenecarboxamide, 6526-67-6; (*E*)-*N,N*-dimethyl-3-phenylpropenamide, 17431-39-9; 2(*S*)-*N*-acetyl-2-phenyl-1,3-oxazolidine, 124619-59-6; (*S*)-phenylglycinol, 20989-17-7; isobutyraldehyde, 78-84-2; 2(*R*)-4(*S*)-2-isopropyl-4-phenyl-1,3-oxazolidine, 124619-60-9; 2(*S*)-4-(*S*)-2-isopropyl-4-phenyl-1,3-oxazolidine, 124619-61-0; 2,2-dimethyl-4-phenyl-1,3-oxazolidine, 124619-62-1; tritylamine, 5824-40-8; 4-methoxybenzyl chloride, 824-94-2; bromoacetic acid ethyl ester, 105-36-2; isoindoline, 496-12-8; β-bromo-*N*-benzylpropionamide, 1665-47-0; bromoacetic acid *tert*-butyl ester, 5292-43-3.

Formation and Homolysis of a Mononuclear Cobalt-Oxygen Adduct

Andreja Bakac* and James H. Espenson*

Contribution from the Ames Laboratory and the Department of Chemistry, Iowa State University, Ames, Iowa 50011. *Received July 31, 1989*

Abstract: The macrocyclic cobalt(II) complex $(H_2O)_nCo(C\text{-}meso\text{-}Me_6[14]aneN_4)^{2+}$ (L^2Co^{2+}) binds oxygen to yield $L^2CoO_2^{2+}$. The rate constants for the binding and release of O_2 in aqueous solutions at 25 °C have values 5.0×10^6 M^{-1} s^{-1} and 1.66×10^4 s^{-1}, respectively. There is no evidence for the formation of a binuclear μ-peroxo complex. The ESR parameters of the oxygen adduct in toluene at 120 K, $g_\parallel = 2.108$, $g_\perp = 1.96$, $A_\parallel = 3.81 \times 10^{-3}$ cm^{-1}, $A_\perp = 2.94 \times 10^{-3}$ cm^{-1}, are consistent with the formulation of the complex as a 1:1 adduct with the unpaired spin density residing on the oxygen. The laser flash photolysis of $L^2CoO_2^{2+}$ (λ_{irr} 490 nm) induces the cleavage of the cobalt-oxygen bond, $L^2CoO_2^{2+} \xrightarrow{h\nu} L^2Co^{2+} + O_2$.

A large number of cobalt-oxygen complexes are known both in solution and in the solid state.[1] The importance of these complexes lies in their being excellent models for metal-dioxygen binding, which should bring about a better understanding of the natural oxygen carriers, such as hemoglobin. Another important aspect of the cobalt-oxygen chemistry deals with the catalytic action of cobalt in the oxidation of a number of organic compounds.[2-4]

The affinity of oxygen for cobalt(II) varies greatly with the solvent and the ligands.[1] Both mononuclear and binuclear complexes are known. The former, usually referred to as superoxo complexes, are often only transients in the formation of the binuclear μ-peroxo complexes, eqs 1 and 2. The assignment of the

$$Co^{II} + O_2 \rightleftarrows Co^{III}O_2 \qquad k_1, k_{-1}, K_1 \qquad (1)$$

$$Co^{III}O_2 + Co^{II} \rightleftarrows Co^{III}O_2Co^{III} \qquad k_2, k_{-2}, K_2 \qquad (2)$$

3+ oxidation state to the cobalt and 1- or 2- to the oxygen is only a formalism of the ionic model, which can by no means account for all the spectral, structural, or chemical properties of these complexes. A better description of binding of O_2 to cobalt(II), at least for the low-spin, five-coordinate Co(II) complexes, is based on the molecular orbital scheme whereby an electron in the d_{z^2} orbital on the cobalt pairs up with an electron in the π^* orbital of O_2.[5]

There exists a wealth of thermodynamic information[1] on dioxygen binding to cobalt, but much less is known about the kinetics

(1) (a) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *79*, 139. (b) Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chem. Rev.* **1984**, *84*, 137. (c) Drago, R. S.; Corden, B. B.; Zombeck, A. *Comments Inorg. Chem.* **1981**, *1*, 53. (d) McLendon, G.; Martell, A. E. *Coord. Chem. Rev.* **1976**, *19*, 1. (e) Martell, A. E. *Acc. Chem. Res.* **1982**, *15*, 155. (f) Vaska, L. *Acc. Chem. Res.* **1976**, *9*, 175. (g) *Oxygen Complexes and Oxygen Activation by Transition Metals*; Martell, A. E., Sawyer, D. T., Eds.; Plenum: New York, 1988. (h) *The Role of Oxygen in Chemistry and Biochemistry*; Ando, W., Moro-oka, Y., Eds.; Elsevier: New York, 1988.

(2) Sheldon, R. A.; Kochi, J. *Metal Catalyzed Oxidations of Organic Compounds*; Academic: New York, 1981; Chapter 4.

(3) (a) Nishinaga, A.; Tomita, H.; Matsuura, T. *Tetrahedron Lett.* **1980**, *21*, 4853. (b) Nishinaga, A.; Tomita, H.; Oda, M.; Matsuura, T. *Tetrahedron Lett.* **1982**, *23*, 339. (c) Nakayama, Y.; Sanemitsu, Y.; Yoshioka, H.; Nishinaga, A. *Tetrahedron Lett.* **1982**, *23*, 2499. (d) Nishinaga, A.; Yamazaki, S.; Matsuura, T. *Tetrahedron Lett.* **1987**, *28*, 6309; **1986**, *27*, 2649. (e) Nishinaga, A.; Kondo, T.; Matsuura, T. *Chem. Lett.* **1985**, 905.

(4) (a) Yamada, A.; Araki, K.; Shiraishi, S. *J. Chem. Soc., Chem. Commun.* **1988**, 530. (b) Skibida, I. P. *Russ. Chem. Rev.* **1985**, *54*, 875.

(5) (a) Tovrog, B. S.; Kitko, D. J.; Drago, R. S. *J. Am. Chem. Soc.* **1976**, *98*, 5144. (b) Bailey, C. L.; Drago, R. S. *Coord. Chem. Rev.* **1987**, *79*, 321.

0002-7863/90/1512-2273$02.50/0