Synthesis of α-hydroxy acid derivatives by the photochemical reaction of *O*-silylchromium(0) carbene complexes and nucleophiles

Benito Alcaide, Luis Casarrubios, Gema Domínguez and Miguel A. Sierra*
Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040 Madrid (Spain)

(Received January 10, 1994)

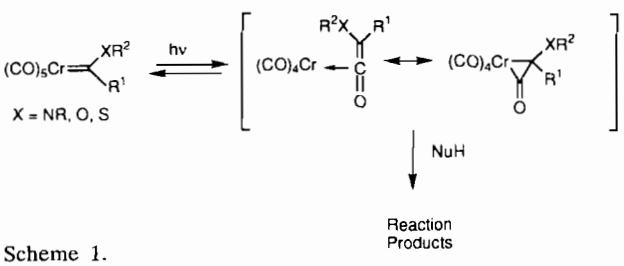
Abstract

N-*p*-Anisyl-α-hydroxy amides are obtained in fair to good yields from pentacarbonyl[(tetramethylammonio)oxy]-carbene chromium(0) complexes in a two step, one pot, process. The reaction involves sequential treatment of the ammonium salts with TMSCl to form pentacarbonyl(silyloxycarbene)chromium(0) complexes, and further irradiation of these complexes in the presence of *p*-anisidine. Additionally, evidence of competitive nucleophile substitution at the carbene carbon by amines and Si–O bond cleavage in silyloxychromium carbene complexes is shown.

Key words: Chromium complexes; Carbene complexes; Amide complexes; Photochemistry

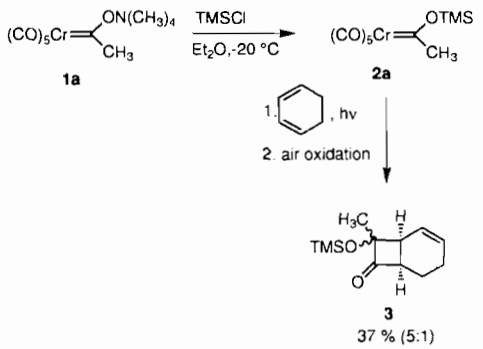
Introduction

Ketene generation by irradiation of heteroatom-stabilized (Fischer) chromium carbene complexes [1], and further reaction of these transient species with different types of nucleophiles has widened the synthetic applications of these interesting metal complexes [2] (Scheme 1). Thus, compounds such as β-lactams [3], cyclobutanones [4], α-amino acids and peptides [5], and aromatic compounds [6], are efficiently produced in the photochemical reactions of these complexes and different types of nucleophiles, either in inter- or intramolecular reactions. Both, alkoxy- and aminochromium(0) carbenes when irradiated with visible light form the transient chromium-coordinate ketenes (even sunlight promotes the reversible insertion of a CO ligand into the Cr–carbene bond). Our interest in this field [7] has led to a series of processes which occur without ketene generation, yet with surprising rate reaction acceleration when the reactions of chromium carbene complexes and dipolar nucleophiles are made under photochemical conditions.



Scheme 1.

The photochemistry of most labile acyl- and silyloxychromium carbene complexes remains almost unexplored. To the best of our knowledge, the sole example is by Hegedus and co-workers [4c] who reported the formation of cyclobutanone **3** by irradiation of pentacarbonyl[(methyl)(trimethylsilyloxy)carbene]chromium(0) (**2a**), generated by reaction of pentacarbonyl[(methyl)[(tetramethylammonio)oxy]carbene]-chromium(0), (**1a**), chlorotrimethylsilane (TMSCl) and 1,3-cyclohexadiene (Scheme 2). Moreover, nucleophile trapping of chromium-coordinated silyloxy ketenes [8]



Scheme 2.

*Author to whom correspondence should be addressed.

SSDI 0020-1693(94)03917-D

would yield hydroxy acid derivatives with an easily removable protecting group, or, depending on the reaction conditions, an unprotected OH group, which may be interesting for some synthetic applications [9]*. We report here the photochemical reactions of different silyloxychromium carbene complexes with amines to give N-substituted α-hydroxy amides in fair to good yields.

Experimental

Melting points were taken on a Büchi 510 apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian XL-300 and a Bruker 250 working at 300 and 250 MHz (^{1}H) and 75 and 62.5 MHz (^{13}C), respectively. Chemical shifts are given in ppm relative to Me_4Si (0 ppm, ^{1}H), $CDCl_3$ (77 ppm, ^{13}C) and DMSO-d_6 (39.7 ppm, ^{13}C). IR spectra were registered on a Perkin-Elmer 781 gratting spectrophotometer. Elemental analyses were obtained by the UCM Microanalysis Service (Facultad de Farmacia, Madrid, Spain).

Irradiations were performed by a 400-W medium-pressure mercury lamp (Applied Photophysics), Pyrex filter and Pyrex well. For purification of crude reaction mixtures by flash chromatography, Merck silica gel (230–400 mesh) was used as the stationary phase. The following chemicals were prepared according to literature procedures: pentacarbonyl[(methyl)[(tetramethylammonio)oxy]carbene]chromium(0) [10], pentacarbonyl[(cyclopropyl)[(tetramethylammonio)oxy]carbene]chromium(0) [11], pentacarbonyl[(butyl)[(tetramethylammonio)oxy]carbene]chromium(0) [10], pentacarbonyl[(phenyl)[(tetramethylammonio)oxy]carbene]-chromium(0) [10], pentacarbonyl[(*p*-anisyl)[(tetramethylammonio)oxy]carbene]chromium(0) [5c], pentacarbonyl[(1-naphtyl)[(tetramethylammonio)oxy]carbene]-chromium(0) [5c], pentacarbonyl[(2-furyl)[(tetramethylammonio)oxy]carbene]chromium(0) [12], pentacarbonyl[(trimethylsilylmethyl)[(tetramethylammonio)oxy]-carbene]chromium(0) [13].

General procedure for preparation of α-hydroxy amides, 8

In an oven-dried 50 ml test tube equipped with a stir bar, 2.0 mmol of the corresponding ammonium salt were placed. The test tube was sealed with a rubber septum and argon was flushed to eliminate traces of oxygen. Anhydrous Et_2O (20 ml) was added, the resulting suspension cooled to 0 °C, and treated with TMSCl (2 mmol, net, dropwise addition via syringe). The resulting heterogeneous mixture was stirred for 1 h at 0 °C, then *p*-anisidine (1.33 mmol) in anhydrous Et_2O (5 ml) was added in one portion, and the stirring stopped. The solution with a solid precipitate was irradiated for 24 h at room temperature under argon. Then, the solvent was removed *in vacuo*, the resulting brown solid was dissolved in EtOAc, filtered through Celite, and air oxidized in an open flask under direct sunlight (preferred) or in a light box (9×20 W fluorescent tubes). Filtration through a short path of Celite of the green–brown precipitate and solvent removal gave the crude compound together with variable amounts of unreacted *p*-anisidine, which was removed by washing with HCl (5%, aqueous solution). The acid treatment usually results in removing of the silyl protecting group, but in some cases additional stirring in the presence of silica gel for 1 h of a Cl_3CH solution of the hydroxyacid was needed. Analytically pure compounds were obtained by flash chromatography or recrystallization.

N-(4-Methoxyphenyl)-2-hydroxy propanamide (8a)

From complex ***1a***. Following the general procedure 0.50 g (1.6 mmol) of complex **1a** and 0.13 g (1.06 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by chromatography (hexane/EtOAc 2:1). White crystalline solid; m.p. 94–95 °C (EtOAc). Yield 0.11 g (50%). ^{1}H NMR ($CDCl_3$) δ: 1.48 (d, 3H, J=6.6 Hz, CH_3), 3.77 (s, 3H, OCH_3), 4.29 (q, 1H, J=6.6 Hz, CH), 6.84 (d, 2H, J=9.1 Hz, arom), 7.43 (d, 2H, J=9.1 Hz, arom), 8.52 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 172.7 (C=O), 156.4, 130.2, 121.5, 114.1 (arom), 68.6 (CH), 55.4 (OCH_3), 21.0 (CH_3). IR (Cl_3CH): ν 3380 (NH, OH), 1675 (C=O), 1535, 1515, 1470, 1445, 1420 cm^{-1}. *Anal.* Calc. for $C_{10}H_{13}NO_3$: C, 61.51; H, 6.72; N, 7.18. Found: C, 61.69; H, 6.45; N, 6.89%.

From complex ***1d***. Following the general procedure 0.79 g (2 mmol) of complex **1d** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by flash chromatography (hexane/EtOAc 2:1). White crystalline solid; m.p. 94–95 °C (EtOAc). Yield 0.19 g (80%). This product was identical to the one obtained from complex **1a**.

N-(4-Methoxyphenyl)-2-hydroxy hexanamide (8b)

Following the general procedure 0.70 g (2 mmol) of complex **1b** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by recrystallization from EtOAc. White crystalline solid; m.p. 98–100 °C (EtOAc). Yield 0.20 g (63%). ^{1}H NMR ($CDCl_3$): δ 0.90 (t, 3H, J=7.2 Hz, CH_3), 1.25–1.44 (m, 4H, Bu), 1.62–1.76 (m, 1H, Bu),

*Analogous reactions using standard alkoxy chromium carbene complexes lead to protected alcohols. The protecting groups are then removed by using conventional deprotecting methodology, for example catalytic hydrogenation for benzyloxy groups.

1.82–1.94 (m, 1H, Bu), 3.48 (bs, 1H, OH), 3.78 (s, 3H, OCH_3), 4.18 (dd, 1H, $J_1=3.9$, $J_2=8.1$ Hz, CH), 6.84 (d, 2H, $J=9.3$ Hz, arom), 7.44 (d, 2H, $J=9.3$ Hz, arom), 8.45 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 172.0 (CO), 156.4, 130.3, 121.5, 114.1 (arom), 72.4 (CH), 55.4 (OCH_3), 34.4, 27.1, 22.4, 13.9 (Bu). IR (Cl_3CH): ν 3370 (NH, OH), 1665 (CO), 1530, 1515, 1465, 1415 cm^{-1}, *Anal.* Calc. for $C_{13}H_{19}NO_3$: C, 65.78; H, 8.07; N, 5.91. Found: C, 65.47; H, 8.31; N, 6.13%.

N-(4-Methoxyphenyl)-2-cyclopropyl-2-hydroxy ethanamide (8c)

Following the general procedure 0.67 g (2 mmol) of complex **1c** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by recrystallization from EtOAc. White crystalline solid; m.p. 128–130 °C (EtOAc). Yield 0.22 g (75%). ^1H NMR ($CDCl_3$): δ 0.45–0.54 (m, 1H, cyclop), 0.56–0.76 (m, 3H, cyclop), 1.14–1.28 (m, 1H, cyclop), 2.90 (bd, 1H, $J=3.6$ Hz, OH), 3.65 (dd, 1H, $J_1=3.6$, $J_2=7.8$ Hz, CH), 3.79 (s, 3H, OCH_3), 6.87 (d, 2H, $J=9.3$ Hz, arom), 7.47 (d, 2H, $J=9.3$ Hz, arom), 8.16 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 170.6 (C=O), 156.4, 130.2, 121.4, 114.1 (arom), 75.2 (CHOH), 55.4 (OCH_3), 15.7, 2.8, 2.0 (cyclopropyl). IR (Cl_3CH): ν 3150, 3280 (NH, OH), 1650 (C=O), 1545, 1520, 1455, 1420 cm^{-1}. *Anal.* Calc. for $C_{12}H_{15}NO_3$: C, 65.13; H, 6.84; N, 6.33. Found: C, 65.35; H, 7.03; N, 6.34%.

N-(4-Methoxyphenyl)-2-hydroxy-2-phenyl ethanamide (8e)

Following the general procedure 0.74 g (2 mmol) of complex **1e** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by recrystallization from EtOAc. White crystalline solid; m.p. 136–138 °C (EtOAc). Yield 0.29 g (86%). ^1H NMR (DMSO-d_6): δ 3.74 (s, 3H, OCH_3), 5.12 (d, 1H, $J=4.6$ Hz, OH), 6.46 (d, 1H, $J=4.6$ Hz, CH), 6.90 (d, 2H, $J=9.0$ Hz, arom), 7.32–7.57 (m, 5H, arom), 7.66 (d, 2H, $J=9.0$ Hz, arom), 9.87 (bs, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 170.8 (C=O), 155.6, 141.2, 131.9, 128.2, 127.7, 126.7, 121.4, 113.9 (arom), 74.1 (CH), 55.3 (OCH_3). IR (KBr): ν 3400, 3250 (NH, OH), 1650 (CO), 1600, 1555, 1515, 1460, 1420 cm^{-1}. *Anal.* Calc. for $C_{15}H_{15}NO_3$: C, 70.01; H, 5.88; N, 5.45. Found: C, 70.16; H, 5.96; N, 5.37%.

N-(4-Methoxyphenyl)-2-(4-methoxyphenyl)-2-hydroxy ethanamide (8f)

Following the general procedure 0.80 g (2 mmol) of complex **1f** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by chromatography (hexane/EtOAc 2:1). White crystalline solid; m.p. 113–115 °C (EtOAc). Yield 0.17 g (45%). ^1H NMR (DMSO-d_6): δ 3.74 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 5.05 (d, 1H, $J=4.8$ Hz, OH), 6.32 (d, 1H, $J=4.8$ Hz, CH), 6.90 (d, 2H, $J=9.0$ Hz, arom), 6.95 (d, 2H, $J=9.0$ Hz, arom), 7.45 (d, 2H, $J=9.0$ Hz, arom), 7.64 (d, 2H, $J=9.0$ Hz, arom), 9.80 (bs, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 171.1 (CO), 158.9, 155.5, 133.3, 131.9, 128.0, 121.3, 113.9, 113.6 (arom), 73.7 (CH), 55.3 (OCH_3), 55.2 (OCH_3). IR (Cl_3CH): ν 3395, 3290 (NH, OH), 1685 (CO), 1615, 1515, 1470, 1415. *Anal.* Calc. for $C_{16}H_{17}NO_4$: C, 66.87; H, 5.97; N, 4.88. Found: C, 67.01; H, 5.95; N, 4.69%.

N-(4-Methoxyphenyl)-2-(α-naphthyl)-2-hydroxy ethanamide (8g)

Following the general procedure 0.84 g (2 mmol) of complex **1g** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by chromatography (hexane/EtOAc 2:1). Colorless oil; yield 0.35 g (85%). ^1H NMR (Cl_3CD): δ 3.70 (s, 3H, OCH_3), 5.82 (s, 1H, CH), 6.81 (d, 2H, $J=9.0$ Hz, arom), 7.42–7.51 (m, 5H, arom), 7.76–7.83 (m, 4H, arom), 8.76 (bs, 1H, NH). ^{13}C NMR (Cl_3CD): δ 169.6 (CO), 156.3, 135.6, 134.0, 133.4, 131.0, 130.5, 129.1, 128.6, 126.3, 125.0, 124.3, 121.1, 114.1 (arom), 74.0 (CH), 55.3 (OCH_3). IR (Cl_3CH): ν 3380 (NH, OH), 1670(CO), 1600, 1515, 1400. *Anal.* Calc. for $C_{19}H_{17}NO_3$: C, 74.24; H, 5.58; N, 4.56. Found: C, 74.01; H, 5.72; N, 4.69%.

N-(4-Methoxyphenyl)-2-(2-furyl)-2-hydroxy ethanamide (8h)

Following the general procedure 0.72 g (2 mmol) of complex **1h** and 0.16 g (1.33 mmol) of *p*-anisidine were irradiated for 24 h. After oxidation the crude amide was purified by chromatography (hexane/EtOAc 2:1). Yellow oil; yield 0.16 g (50%). ^1H NMR ($CDCl_3$): δ 3.80 (s, 3H, OCH_3), 5.26 (s, 1H, CH), 6.38 (dd, 1H, $J_1=2.1$, $J_2=3.5$ Hz, Fu), 6.46 (d, 1H, $J=3.5$ Hz, Fu), 6.87 (d, 2H, $J=9.0$ Hz, arom), 7.42 (dd, 1H, $J_1=0.9$, $J_2=2.1$ Hz, Fu), 7.46 (d, 2H, $J=9.0$ Hz, arom), 8.22 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 167.4 (C=O), 156.4, 151.4, 143.1, 128.3, 121.6, 114.2, 110.7, 108.9 (arom), 68.2 (CH), 55.4 (OCH_3). IR (Cl_3CH): ν 3395, 3300 (NH, OH), 1685, 1660 (C=O), 1520, 1470, 1425 cm^{-1}. *Anal.* Calc. for $C_{13}H_{13}NO_4$: C, 63.14; H, 5.30; N, 5.67. Found: C, 63.25; H, 5.42; N, 5.75%.

General procedure for the thermal reactions of complexes 2 and alcohols or amines

In an oven-dried 100 ml round bottom flask equipped with a stir bar, 2.0 mmol of the corresponding ammonium salt were placed. The flask was sealed with a rubber septum and argon was flushed to eliminate traces of oxygen. Anhydrous Et_2O (20 ml) was added and the resulting suspension cooled to 0 °C, and treated with TMSCl (2 mmol, net, dropwise addition via syringe).

The heterogeneous mixture was stirred for 1 h at 0 °C, and the nucleophile (1.33 mmol) was added in ether (5 ml). The resulting solution was placed in the dark and stirred for 24 h under argon at room temperature. Treatment of the crude reaction mixture was similar to that used for preparation of the amides **8**. The crude reaction material was analyzed by ^{1}H NMR, unambiguously confirming the presence of benzoic acid and/or unreacted nucleophile as the only organic materials. Except for amide **8a** further purification was not carried out.

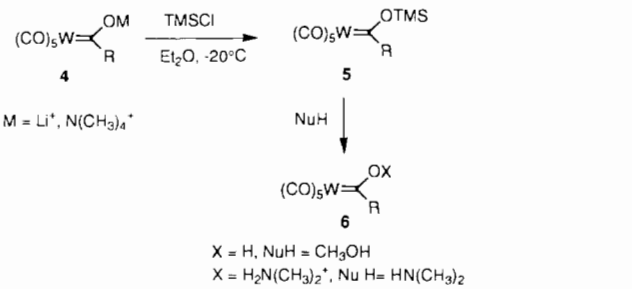
N-Benzyl ethanamide (7a)

Following the general procedure 0.62 g (2 mmol) of complex **1a** and 0.14 g (1.33 mmol) of benzyl amine were reacted for 24 h. After oxidation, pure amide **7a** was obtained by flash chromatography (hexane/EtOAc 1:1) as a colorless crystalline solid; m.p. 60–61 °C, lit. [14] 61 °C. Yield 0.07 g (35%).

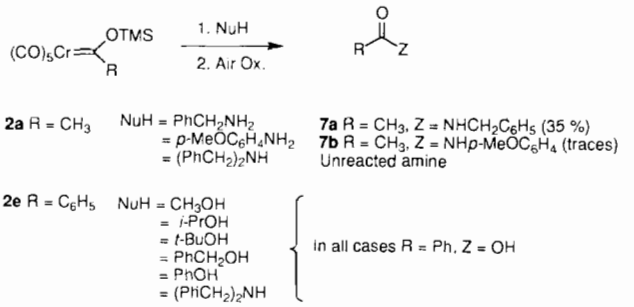
Results and discussion

Two main problems have to be resolved in order to use silyloxychromium carbene complexes as ketene precursors: first, to achieve their quantitative generation in the photolysis conditions, and, second, to avoid the competitive silyloxy group cleavage or substitution at the carbene carbon by the nucleophile. Fischer *et al.* [15] have reported the synthesis of silyloxytungsten **5** and chromiumcarbene complexes **2** following two different routes, namely, by *in situ* trapping of the lithium salt formed by addition of an organolithium to $M(CO)_6$ (M = W, Cr) with TMSCl, or by carrying out the same reaction with the most easily handled ammonium salts, **1** and **4**. We chose the second option, and tuned up the conditions to effectively, *in situ*, silylate these chromium carbene salts. Among the different reaction conditions used, best results were obtained by working in ether at 0 °C, using TMSCl as the silylating agent. Other solvents (DCM, THF, etc.), and silylating agents (TBDMSCl, TESCl) gave poor conversions to the desired complexes even after long reaction times. Therefore, treatment of the corresponding ammonium salts with an equimolar amount of TMSCl at 0 °C in ether for an hour yields the desired trimethylsilyloxychromium carbenes, **2**, which are stable for days in solution under argon, but decompose in minutes at room temperature, upon solvent elimination even under argon. Thus, complexes **2** were generated *in situ* and used in solution without further purification.

Competence between Si–O bond cleavage and nucleophile substitution at the carbene carbon was next addressed. It has been reported [15, 16] that the Si–O bond in tungsten complexes **5** is broken by alcohols and secondary amines, due to the shift of electron density from the oxygen to the carbene atom, making the silicon atom more accessible to nucleophiles and, therefore, competing successfully with attack to the carbene carbon (Scheme 3). Our own results using chromium complexes **2** and alcohols confirm the results obtained with the tungsten analogs. Thus, complex **2e** was reacted in the dark with primary, secondary, tertiary alcohols (MeOH, $PhCH_2OH$, Pr^iOH, Bu^tOH) and phenol, to yield, upon air oxidation, benzoic acid as the sole organic material. Analogous results were obtained in the reaction of this complex and dibenzyl amine. However, when complex **2a** was reacted with benzyl amine under analogous conditions, *N*-benzyl ethanamide (**7a**) was the reaction product, together with unreacted benzyl amine. Less basic, *p*-anisidine forms in its reaction with complex **2a** traces of *N-p*-anisyl ethanamide (**7b**) together with unreacted amine*. The results of these reactions are summarized in Scheme 4. Formation of ethanamides **7a**, **7b**, show that, at least for more basic, sterically unhindered nucleophile



Scheme 3.



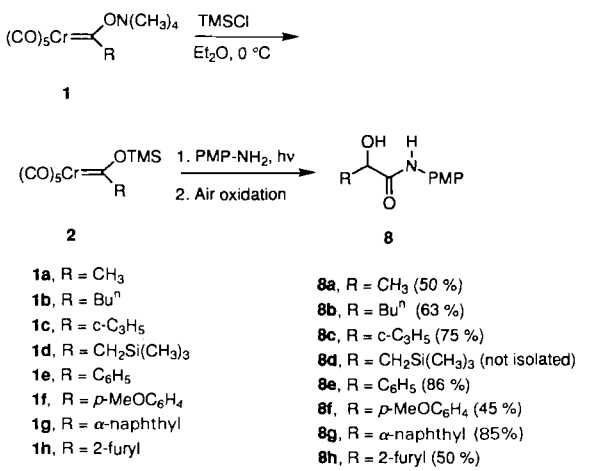
Scheme 4.

*Although improbable, acetamides **7a** and **7b** may be formed by reaction of acetic acid and the amines during the oxidation process. To eliminate this eventuality complex **1e** was silylated and treated with MeOH, and irradiated under standard conditions. Equimolar amounts of acetic acid and benzyl amine were added to the ethereal solution prior to oxidative work-up, and the resulting mixture was oxidized. Neither amide **7a** nor *N*-benzyl benzamide were detected in the crude reaction mixture (^{1}H NMR). Therefore, amides **7** should be formed through the pathway discussed above.

amines, substitution at the carbene carbon may compete with Si–O bond cleavage.

From our own results and the literature background, it is clear that, in order to obtain ketene derived products, alcohols are not adequate nucleophiles, and a careful choice has to be made for amines. In fact, in the preliminary photochemical runs using complex **1a** and benzylamine as the nucleophile, *N*-benzyl ethanamide (**7a**) was the sole reaction product. Therefore, nucleophile substitution, and probably Si–O bond cleavage, are faster than CO insertion and further ketene trapping, at least in the conditions we used. The more hindered dibenzyl amine produces no other organic isolable material but unreacted amine. Irradiation in the presence of alcohols results, exclusively, in products derived from Si–O bond cleavage. By switching to a less nucleophile amine, namely *p*-anisidine, we obtained the adequate balance between nucleophile substitution at the carbene carbon, Si–O bond cleavage, and the ability to trap the photochemically generated ketene. In fact, sequential treatment of ammonium salt **1** in ether at 0 °C with TMSCl for 1 h, followed by addition of the amine and irradiation, yields upon oxidation hydroxy amides **8** in fair to good yields (Scheme 5). Reaction mixtures are extremely clean, unreacted *p*-anisidine is the sole contaminant and it can be eliminated by washing the reaction crude with diluted HCl. The acidic treatment simultaneously eliminates the silicon protected amides, which are obtained together with amides **8** in variable amounts.

A wide variety of complexes **1** can be converted to amides **8**. The reaction tolerates aliphatic, cycloaliphatic, aromatic and heteroaromatic substituents attached to the carbene carbon. The reaction of complex **1d** deserves some additional comments. Complex **1d** undergoes a clean transformation to the amide **8a** (80%), the sole organic material detected in the crude mixtures. Amide **8a** may be formed by loss of the silicon group during



Scheme 5.

isolation. Any attempts to isolate the parent amide **8d**, by working in strictly neutral conditions, were fruitless.

In conclusion, the results above show that O-silylated complexes **2** are suitable substrates for ketene generation, even with nucleophiles which, in principle, may promote Si–O bond cleavage, allowing α-hydroxy amides **8** to be obtained in good yields, from easily available ammonium salts, **1**, in a two step, one pot reaction. Additionally, competition between nucleophile substitution at the carbene carbon and Si–O bond breakage in complexes **2** has been observed for the first time, when basic, sterically unhindered amines are used. Studies of this process, and the thermal and photochemical behavior of complexes **2** with other nucleophiles, are currently underway in our laboratories.

Acknowledgements

This work was supported by the DGICYT (MEC-Spain, Grant PB90-0047) and CAM (Madrid-Spain, Grant 290/92). Mr J. Pérez-Castells is gratefully acknowledged for a careful revision of the manuscript.

References

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

2 (a) W.D. Wulff, in B.M. Trost and I. Fleming (eds.), *Comprehensive Organic Synthesis*, Vol. 5, Pergamon, New York, 1991, pp. 1065–1113; (b) K.H. Dötz, in H. tom Dieck and A. de Meijere (eds.), *Organometallics in Organic Synthesis: Aspects of a Modern Interdisciplinary Field*, Springer, Berlin, 1988; (c) K.H. Dötz, *Angew. Chem., Int. Ed. Engl., 23* (1984) 587.

3 (a) P.J. Colson and L.S. Hegedus, *J. Org. Chem., 58* (1993) 5918; (b) Y. Narukawa, K.N. Juneau, D. Snustad, D.B. Miller and L.S. Hegedus, *J. Org. Chem., 57* (1992) 5453; (c) B. Alcaide, G. Domínguez, J. Plumet and M.A. Sierra, *J. Org. Chem., 57* (1992) 447; (d) C. Betschart and L.S. Hegedus, *J. Am. Chem. Soc., 114* (1992) 5010; (e) L.S. Hegedus, R. Imwinkelried, M.A. Sargent, D. Dvorak and Y. Satoh, *J. Am. Chem. Soc., 112* (1990) 1109.

4 (a) L.S. Hegedus, R.W. Bates and B.C. Söderberg, *J. Am. Chem. Soc., 113* (1991) 924; (b) B.C. Söderberg and L.S. Hegedus, *J. Org. Chem., 56* (1991) 2209; (c) B.C. Söderberg, L.S. Hegedus and M.A. Sierra, *J. Am. Chem. Soc., 112* (1990) 4364; (d) M.A. Sierra and L.S. Hegedus, *J. Am. Chem. Soc., 111* (1989) 2335.

5 (a) S.R. Pulley and L.S. Hegedus, *J. Am. Chem. Soc., 115* (1993) 9037; (b) E. Lastra and L.S. Hegedus, *J. Am. Chem. Soc., 115* (1993) 87; (c) J.M. Vernier, L.S. Hegedus and D.B. Miller, *J. Org. Chem., 57* (1992) 6914; (d) L.S. Hegedus, E. Lastra, Y. Narukawa and D.C. Snudstad, *J. Am. Chem. Soc., 114* (1992) 2991; (e) L.S. Hegedus, M.A. Schwindt, S. DeLombaert and R. Imwinkelried, *J. Am. Chem. Soc., 112* (1990) 2264.

6 (a) C.A. Merlic, D. Xu and S.I. Khan, *Organometallics, 11* (1992) 412; (b) C.A. Merlic and D. Xu, *J. Am. Chem. Soc., 113* (1991) 7418.

7 (a) B. Alcaide, L. Casarrubios, G. Domínguez and M.A. Sierra, *J. Org. Chem., 58* (1993) 3886; (b) B. Alcaide, G. Domínguez, J. Rodríguez-López and M.A. Sierra, *Organometallics, 11* (1992) 1979; (c) B. Alcaide, G. Domínguez, J. Plumet and M.A. Sierra, *Organometallics, 10* (1991) 11.

8 R.S. Ward, in S. Patai (ed.), *Chemistry of Ketenes, Allenes and Related Compounds*, Vol. 1, Wiley, Chichester, UK, 1980, pp. 223–273.

9 (a) D. Seebach, in R. Scheffold (ed.), *Modern Synthetic Methods*, Springer, Frankfurt, 1980, p. 91; (b) K. Mori, in J. ApSimon (ed.), *The Total Synthesis of Natural Products*, Vol. 4, Wiley, New York, 1981, p. 1.

10 E.O. Fischer and A. Maasböl, *Chem. Ber., 100* (1967) 2445.

11 J.A. Connor and E.M. Jones, *J. Chem. Soc., Dalton Trans.,* (1973) 2119.

12 J.A. Connor and E.M. Jones, *J. Chem. Soc. A,* (1971) 1974.

13 B.C. Söderberg and B.A. Bowden, *Organometallics, 11* (1992) 2220.

14 *Handbook of Chemistry and Physics*, CRC Press, Boca Raton, FL, 1st Student edn., 1990.

15 E.O. Fischer, T. Selmayr, F.R. Kreissl and U. Schubert, *Chem. Ber., 110* (1977) 2574.

16 E.O. Fischer, U. Schubert and H. Fischer, *Pure Appl. Chem., 50* (1978) 857.