Tetrahedron Letters,Vol.30,No.31,pp 4061-4064,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Maxwell Pergamon Macmillan plc

ALKYLATIONS OF "ENOLATES" GENERATED FROM AMINO CARBENE COMPLEXES OF CHROMIUM

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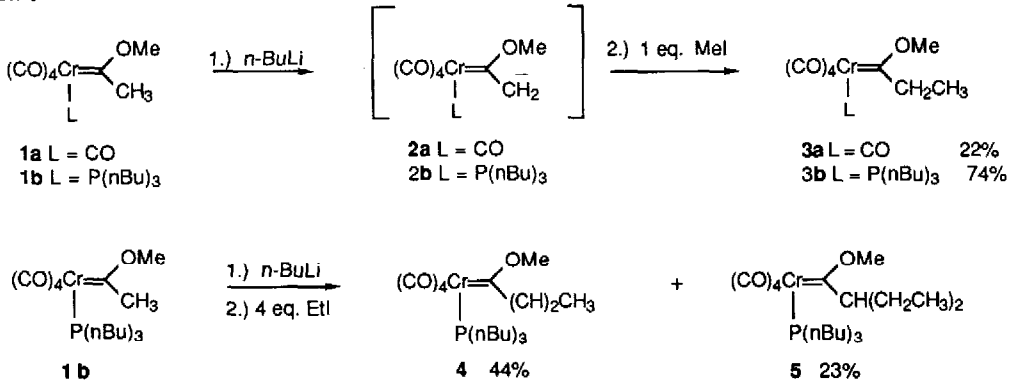
Abstract: The carbanion generated from the methyl (pyrrolidino) chromium carbene complex **6a** reacts with a variety of alkylating reagents to provide good to high yields of monoalkylated products. The alkylation reactions of the amino carbene complex were found to be significantly more efficient than alkoxy carbene complex analogs. Dialkylation was not detected and might be explained by the observed sluggish alkylation of the ethyl (pyrrolidine) carbene complex **6b**.

The synthetic utility of transition metal alkoxy carbene complexes has been well established over the past twenty years.[1] Instrumental to the continuing applications of alkoxy carbene complexes in organic chemistry have been the general methods for elaborating the carbene ligand. Casey has demonstrated that reactions of the alkoxy carbene anion **2a** can yield carbene complexes not readily available by traditional routes.[2] More recently amino carbene complexes have emerged as versatile reagents for organic synthesis.[3] In order to take full advantage of the reactivity of amino carbene complexes, it has become necessary to investigate routes toward elaboration of the carbene ligand. Alkylations of amino carbene complexes at nitrogen appeared early in the literature and more recently Casey demonstrated alkylations at the carbon α to nitrogen on aryl (amino) complexes.[4,5] There have been no reports in the literature however, of the generation of the anion at the carbon α to the carbene carbon of amino carbene complexes or of any subsequent treatment with electrophiles.[6]

Scheme 1

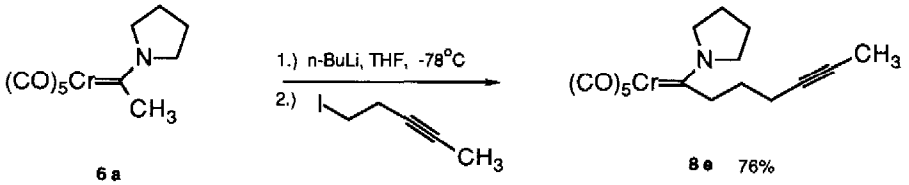


The protons on carbons α to the carbene carbon of Fischer type alkoxy complexes have been shown to be both extremely thermodynamically (pK_a = 8) and kinetically acidic.[7,8] As a consequence of the stability of **2a**, Casey has

found that only the most reactive electrophiles lead to products.[2] Methyl iodide and other primary halides give either poor yields of alkylated product or fail to react with **2a**.[9] Alkylations with allylic and benzylic halides give improved yields but this is offset by severe problems with dialkylation.[9a] In a previous report from this laboratory, it was demonstrated that replacement of a CO ligand of the pentacarbonyl complex **1a** with tri-n-butylphosphine resulted in a complex **1b** that was six orders of magnitude less acidic than **1a**.[10] The corresponding anion **2b** displays a marked increase in its reactivity with alkylating reagents. A three fold increase in the yield of the alkylation product is realized for the reaction of **2b** with methyl iodide as compared to the reaction of **2a** under similar conditions. The generality of the enhanced reactivity of **2b** was surveyed and it was observed that although the reaction of **2b** with ethyl triflate gave high yield of the propyl complex **4**, ethyl halides gave only moderate yields and were accompanied by significant amounts of the dialkylated product **5**.

It was anticipated the anion derived from dialkylamino carbene complexes might display enhanced reactivity similar to the tri-n-butylphosphine carbene anions. Indeed it has been found the anion **7a** generated from the pyrrolidino carbene complex **6a**[11] reacts with a variety of alkylating agents to give the expected products in uniformly high yield. The procedure is typified by the reaction of complex **6a** with 1-iodo-3-pentyne. A 25 mL single-necked round bottom flask was charged with 0.99 g (3.4 mmol) of complex **6a** and a teflon coated stir bar and then fitted with a rubber septum. The flask was evacuated and then refilled with argon. The solvent was then injected by syringe (THF, 8 mL) and the resulting yellow solution was then cooled to -78° C. A solution of *n*-butyllithium in hexanes (2.15 mL, 1.6 M) was added at -78° C to generate the anion **7a**. After 20 min, 0.78 g (4.0 mmol, 1.1equiv) of 1-iodo-3-pentyne was added in one portion. The -78° C cooling bath was replaced with an ice water bath and stirring was continued for 1h. The reaction was quenched with 5% sodium bicarbonate. The mixture was diluted with ether and transferred to a separatory funnel and the solution was washed with distilled water and brine. The organic solution was dried over magnesium sulfate, filtered through a plug of Celite and concentrated on a rotorary evaporator. The resulting oil was purified by column chromatography on silica gel in the presence of air with a benzene : hexane (1: 5) solution to provide 0.93g of the alkylation product **8e** (76 % yield).

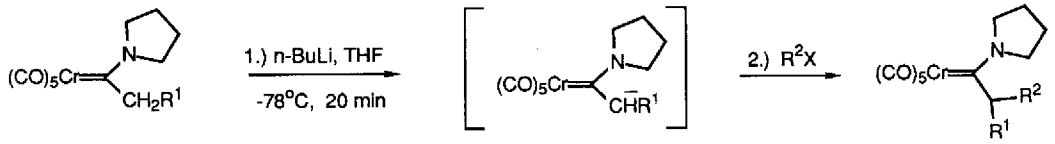
Scheme 2



6a **8e** 76%

Methyl triflate, the most efficient alkylating reagent for alkoxy carbene complexes, gives high yield of the ethyl complex with amino complexes as well (Table 1). Unlike the reactions with alkoxy complexes, alkyl halides were found to be generally useful alkylating reagents for the pyrrolidino carbene complex. Alkyl iodides and ethyl bromide gave high yields of alkylated product. The secondary alkyl halide 2-iodopropane was also found to provide a synthetically useful yield of the alkylated product. Alkyl tosylates were investigated and although it was observed that alkylation products were obtained, the reactions failed to go to completion under the conditions described in Table 1. Contrary to the successful reactions of primary alkyl iodides and bromides, no alkylation product was observed for the reaction of **7a** with 1-chloropropane.

Notably, throughout this study dialkylated products were never detected. This is particularly significant for the examples of the ethyl and the benzyl halides for which considerable dialkylation was observed for the alkylations of alkoxy complexes **1b** (scheme 1) and **1a** .[9a, 11] The lack of dialkylation might be explained by the apparently more sluggish reactivity of substituted (amino) carbene anions. This is supported by attempted alkylations of the ethyl complex **6b.**



6a $R^1 = H$
6b $R^1 = CH_3$

7a $R^1 = H$
7b $R^1 = CH_3$

8

Table I. Alkylations of pyrrolidino chromium carbene complexes

entry	complex	R^2X[a]	Conditions[b]	product	% yield	% recvry of **6**
1	**6a**	MeOTf[c]	-78°C, 5 min	**8a**	89	
2	**6a**	MeI	0°C, 20 min	**8a**	86	
3	**6a**	CH_3CH_2I	0°C, 20 min	**8b**	95	
4	**6a**	CH_3CH_2Br	0°C, 40 min	**8b**	87	
5	**6a**	CH_3CH_2OTs	RT, 4h	**8b**	73[g]	9
6	**6a**	$CH_3(CH_2)_2Cl$[d]	0°C, 30 min RT, 60 min	**8c**	0	59
7	**6a**	$(CH_3)_2CHI$	0°C, 90 min - RT, 90 min	**8d**	67	8
8	**6a**	$CH_3C{\equiv}C(CH_2)_2I$[e]	0°C, 1 h	**8e**	76	
9	**6a**	$CH_3C{\equiv}C(CH_2)_2OTs$[e]	0°C, 2 h - RT, 3 h[f]	**8e**	36[g]	21
10	**6a**	$PhCH_2Br$	-78°C 20 min- 0°C, 40 min	**8f**	66	
11	**6b**	MeOTf[c]	-78°C, 5 min	**8g**	12[g]	66
12	**6b**	MeOTf[c]	-78°C, 5 min 0°C, 10 min	**8g**	28[g]	58
13	**6b**	MeI[d]	0°C, 2 h - RT, 3 h	**8g**	44[g]	41

[a]Unless otherwise indicated all reactions run with 2 equiv of alkylating reagent. [b]Unless otherwise specified all reaction concentrations were between 0.1M and 0.17M in **6**. [c]1.3 equiv. [d]5 equiv. [e]1.1 equiv. [f]2.3 M in **6**. [g]Product isolated as a mixture with starting material.

While the methyl (pyrrolidino) complex **6a** reacted rapidly with both methyl triflate and methyl iodide, more forcing conditions failed to provide similar results for the ethyl complex **6b** which gave only modest yields of the alkylation product **8g**.

This study has revealed dramatic differences in the alkylations of amino carbene complexes and alkoxy complexes. In contrast to alkoxy complexes, "enolates" generated from amino complexes can be alkylated in high yields with both primary and secondary alkyl halides and without any competing dialkylation. Alkylation methods, thus should provide entry to a variety of amino complexes not readily accessible by traditional methods.

Acknowledgment. This work was supported by the National Institutes of Health (PHS-GM 33589). The NMR instruments used were funded in part by the NSF Chemical Instrumentation Program and by the NCI via the University of Chicago Cancer Research Center (CA-14599).

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(Received in USA 19 April 1989)