Fischer chromium carbene complexes as nucleophiles in palladium-catalyzed allylic substitution reactions

Dušan Drahoňovský,[a] Vincent Borgo[b] and Dalimil Dvořák[a],*

[a]*Department of Organic Chemistry, Prague Institute of Chemical Technology, Technická 5, 166 28 Prague 6, Czech Republic*
[b]*Université Blaise Pascal Clermont-Ferrand II, 34, avenue Carnot, B.P. 185, 63006 Clermont-Ferrand cedex 1, France*
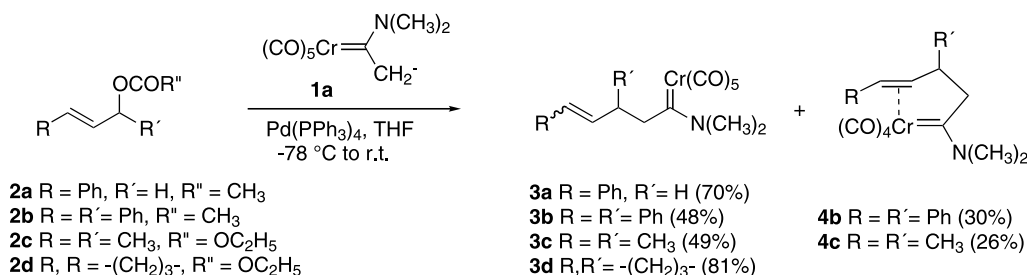
Abstract—The Pd-catalyzed reaction of carbanions derived from chromium aminocarbene complexes with allylic acetates and carbonates smoothly affords the corresponding allyl-substituted aminocarbenes. On the contrary, the same reaction of the anion derived from pentacarbonyl[(methoxy)methylcarbene]chromium(0) with cinnamyl acetate affords 5-methoxy-1-phenylhexa-1,5-diene, the product of 1-methoxyethen-1-yl group transfer. © 2002 Elsevier Science Ltd. All rights reserved.

Alkylation of allylic substrates by stabilized carbanions is one of the synthetically most useful reactions catalyzed by palladium(0) complexes.[1] A wide range of allylic substrates and nucleophiles undergo this reaction making this an important process for the formation of carbon–carbon bonds. The most commonly used nucleophiles are 'soft' stabilized carbanions, such as dimethyl malonate. Also, nitrogen, sulfur, oxygen, phosphorus and silicon nucleophiles, hydrides, organometallics and many others have been employed successfully.[2]

Alkoxy- and aminocarbene complexes of chromium have been shown to undergo self dimerization and C–H insertion reactions catalyzed by $Pd(OAc)_2$,[3,4] while chromium allyloxy(aryl)carbene complexes undergo formal [2,3]- or [1,2]-sigmatropic rearrangement on treatment with a catalytic amount of $Pd(PPh_3)_4$ under CO atmosphere.[5] Pd(0)-catalyzed reactions of acylchromate complexes have been used for the preparation of allylic ketones[6] and α-diketones[7] and for a double acylation of alkenes.[8] In this context, it is rather surprising that the highly stabilized anions generated from Fischer carbenes[9] have not been used for this type of transformation. If successful, this reaction would open a new route to highly substituted unsaturated Fischer carbenes.[10,11] Herein, we wish to report our results in the application of Fischer amino- and alkoxycarbene complexes of chromium in Pd-catalyzed allylic substitution reactions.

Since the anions derived from aminocarbenes are known to be more nucleophilic than their alkoxy counterparts, we first attempted the reaction of pentacarbonyl[(N,N-dimethylamino)(methyl)carbene]chromium-(0) (**1a**).[12] The anion of **1a** was generated in THF by treatment with n-BuLi, then cinnamyl acetate **2a**,


2a R = Ph, R′ = H, R″ = CH_3
2b R = R′ = Ph, R″ = CH_3
2c R = R′ = CH_3, R″ = OC_2H_5
2d R, R = -$(CH_2)_3$-, R″ = OC_2H_5

3a R = Ph, R′ = H (70%)
3b R = R′ = Ph (48%)
3c R = R′ = CH_3 (49%)
3d R,R′ = -$(CH_2)_3$- (81%)

4b R = R′ = Ph (30%)
4c R = R′ = CH_3 (26%)

Scheme 1.

* Corresponding author. Fax: +420-2-24354288; e-mail: dvorakd@vscht.cz

followed by Pd(PPh$_3$)$_4$ (1 mol%) were added at −78°C. After allowing the reaction mixture to warm to room temperature, palladium black precipitated and allyl-aminocarbene **3a** was obtained in 70% yield (Scheme 1).

1b   **6a**   **7a**
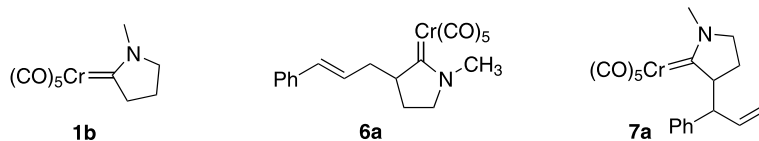
Only *n*-BuLi proved to be effective in the formation of anion **1a**. Attempts to run the reaction of **1a** using *t*-BuOK, Et$_3$N, NaH or carrying out the reaction in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) failed. Similarly, the reaction of cinnamic carbonate, performed in the absence of palladium catalyst or without the added base, was unsuccessful. Interestingly, the reaction proceeds very easily, and was accomplished within 2 h even at −5°C. The nature of the palladium catalyst does not influence the outcome of the reaction significantly since all palladium catalysts gave approximately the same isolated yield of **3a** [Pd(PPh$_3$)$_4$ (73%); PdCl$_2$(PPh$_3$)$_2$, (70%); Pd$_2$dba$_3$·CHCl$_3$/1,1′-bis(diphenyl-phosphino)ferrocene (68%)].[†]

Secondary allylic acetates and carbonates **2b–d** also reacted with **1a**. In the case of acyclic acetate **2b** and carbonate **2c**, an approximately 1:1 mixture of the expected product of allylic substitution **3b** or **3c** and the corresponding chelated alkene–carbene complex **4b** or **4c** were obtained (Scheme 1). The chelation is reversible and under CO atmosphere (1 atm) the chelates **4b** and **4c** were quantitatively converted into the nonchelated complexes **3b** and **3c**. Attempts to avoid the formation of the chelated complexes by running the substitution reaction under a CO atmosphere were unsuccessful. The reaction was completely inhibited by the presence of CO gas (1 atm). Chelation was not observed with aminocarbene **3d**, which is the only carbene product isolated from the reaction of cyclohexenyl carbonate (**2d**) with aminocarbene **1a**.
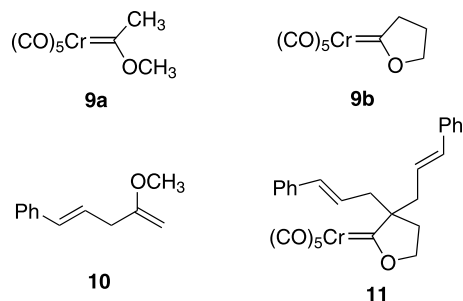
The cyclic aminocarbene complex **1b**[12] also reacted with

2a. Besides the linear product **6a** the formation of a small amount (<10%) of the branched carbene **7a** was also observed in the reaction catalyzed by PdCl$_2$(PPh$_3$)$_2$.

Reaction of the anion of pentacarbonyl[(methoxy)-methylcarbene]chromium(0) (**9a**)[13] with cinnamic acetate (**2a**) did not lead to any carbene product. Instead, a non-conjugated enol ether **10**, the product of alkoxyvinyl group transfer, was obtained.[‡] Secondary allylic substrates **2b**, **2c** and **2d** did not react with **9a** under the above conditions.[§]

With the cyclic alkoxycarbene complex **9b**[14] the only product obtained was dialkylated carbene **11** (21%), even when the ratio of **2a** to **9b** was 1:1. In the case when the ratio of **2a** to **9b** was 2:1, the dialkylated product **11** was isolated in 50% yield.[¶]

9a   **9b**

10   **11**

[†] *Representative procedure:* To a precooled (−78°C) solution of **1a** (345 mg, 1.3 mmol) in THF (4 mL), *n*-BuLi (0.9 mL, 1.6 M solution) was added. The solution was maintained at −78°C for 15 min, then cinnamyl acetate **2a** (211 mg, 1.2 mmol) in THF (1.5 mL) and (PPh$_3$)$_2$PdCl$_2$ (8.4 mg, 0.012 mmol) in THF (2 mL) were successively added. The resulting mixture was allowed to warm to room temperature; after 2 h the mixture was filtered through Celite and the solvent was evaporated. Chromatography on silica gel (petroleum ether/dichloromethane, 2:1) afforded **3a** as pale yellow solid (319 mg, 70%), which decomposed without melting above 130°C. ^{1}H NMR δ 1.90 (m, 2H, =CH-CH$_2$), 1.94 (s, 3H, N-CH$_3$), 2.83 (m, 2H, -CH$_2$-C=Cr), 3.00 (s, 3H, N-CH$_3$), 5.95 (m, 1H, =CH-CH$_2$), 6.31 (d, *J*=15.8 Hz, 1H, Ph-CH=), 7.06 (m, 1H, PhH), 7.14 (m, 2H, PhH), 7.19 (m, 2H, PhH). ^{13}C{1H} NMR δ 28.4 (=CH-CH$_2$), 40.7 (N-CH$_3$), 51.8 (-CH$_2$-C=Cr), 52.3 (N-CH$_3$), 126.4 (=CH-), 127.3, 127.6, 128.8 (5×CH, Ph), 131.6 (Ph-CH=), 137.2 (C$_{ipso}$, Ph), 218.5, 223.2 (5×CO), 274.4 (Cr=C<). IR (CHCl$_3$) *v* 1529 (w), 1924 (s), 1968 (w), 2058 (m) cm^{-1}. Anal. calcd for C$_{18}$H$_{17}$CrNO$_5$: C, 57.99; H, 4.52; N, 3.69. Found: C, 58.05; H, 4.72; N, 3.63.

[‡] The same procedure as described for the preparation of **3a** gave after chromatography (petroleum ether/dichloromethane, 2:1, 1% of Et$_3$N) **10** (34%) as a colorless oil. ^{1}H NMR δ 3.01 (d, *J*=7.2 Hz, 2H, =CH-CH$_2$-), 3.58 (s, 3H, -OCH$_3$), 3.96 (m, 2H, -C=CH$_2$), 6.28 (m, 1H, =CH-CH$_2$-), 6.46 (d, *J*=15.4 Hz, 1H, Ph-CH=), 7.20–7.40 (m, 5H, Ph-). ^{13}C{1H} NMR δ 38.5 (=CH-CH$_2$-), 54.9 (-OCH$_3$), 81.2 (-C=CH$_2$), 126.1 (=CH-CH$_2$-), 126.4, 127.1, 128.4 (5×CH, Ph), 131.7 (Ph-CH=), 137.5 (C$_{ipso}$, Ph-), 162.7 (-CH$_2$-C=). IR (CHCl$_3$) *v* 966 (s), 1071 (s), 1180 (s), 1273 (s), 1450 (m), 1595 (m), 1639 (s), 1675 (m), 1715 (s), 2838 (w), 2957 (m), 3020 (s), 3069 (w), 3089 (w) cm^{-1}. MS-FAB (*m/z*) 175.0 [*M*+H]. When the chromatography was performed without Et$_3$N, 6-phenylhex-5-en-2-one,[15] the product of hydrolysis of **10** was isolated in 41% yield. ^{1}H NMR δ 2.22 (s, 3H, -CH$_3$), 3.34 (d, *J*=7.1 Hz, 2H, =CH-CH$_2$-), 6.33 (m, 1H, =CH-CH$_2$-), 6.48 (d, *J*=15.9 Hz, 1H, Ph-CH=), 7.24 (m, 1H, PhH), 7.31 (m, 2H, PhH), 7.38 (m, 1H, PhH).

[§] From the mechanistical point of view, the initially formed π-allyl palladium complex can react with the anion of **9a** which acts as 'Cr-nucleophile' with subsequent reductive elimination of Cr. Transmetallation of the enol ether group to the palladium of the above π-allyl palladium complex followed with reductive elimination is another possibility.

[¶] Double alkylation of Fischer carbenes is relatively common and is ascribed to the higher reactivity of α-substituted carbene complexes.[16] However, the difference in reactivity between **9a** and **9b** remains unclear.

In conclusion, carbanions derived from chromium aminocarbene complexes react easily with allylic acetates and carbonates giving allyl-substituted aminocarbenes. Alkoxycarbenes behave differently, thus carbanions derived from the pentacarbonyl-[(methoxy)methylcarbene]chromium(0) **9a** transfer an alkoxyalkenyl group, while cyclic chromium alkoxycarbene **9b** gives the dialkylated alkoxycarbene **12**, exclusively. A continued study of this reaction including its enantioselective version and mechanistical aspects are currently underway.

Acknowledgements

References

1. For reviews see: (a) Harrington, P. M. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Elsevier Science: Oxford, UK, 1995; Vol. 12, pp. 797–904; (b) Hegedus, L. S. In *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Sausalito, California, 1999; pp. 250–275.

2. For a review on the different nucleophiles employed see: (a) Godleski, S. A. In *Comprehensive Organic Synthesis* 4; Trost, B. M., Ed.; Pergamon Press: Oxford 1991, p. 585. See also the reference section in: (b) Starý, I.; Zajíček, J.; Kočovský, P. *Tetrahedron* **1992**, *48*, 7229.

3. Sierra, M. A.; Mancheño, M. J.; Sáez, E.; del Amo, J. C. *Am. Chem. Soc.* **1998**, *120*, 6812.

4. Sierra, M. A.; del Amo, J. C.; Mancheño, M. J.; Gómez-Gallego, M. *J. Am. Chem. Soc.* **2001**, *123*, 851.

5. Sakurai, H.; Tanabe, K.; Narasaka, K. *Chem. Lett.* **1999**, 75.

6. Sakurai, H.; Tanabe, K.; Narasaka, K. *Chem. Lett.* **1999**, 309.

7. Sakurai, H.; Tanabe, K.; Narasaka, K. *Chem. Lett.* **2000**, 168.

8. Yamane, M.; Ishibashi, Y.; Sakurai, H.; Narasaka, K. *Chem. Lett.* **2000**, 174.

9. Fischer, E. O. *Pure Appl. Chem.* **1970**, *24*, 407.

10. Very recently it was shown, that these types of γ,δ-unsaturated chromium carbene complexes can be prepared by cross metathesis reactions: Zhang, L.; Herndon, W. *Tetrahedron Lett.* **2002**, *43*, 4471.

11. For reviews on the reactivity of carbene complexes see: (a) Hegedus, L. S. In *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Sausalito, California, 1999; pp. 143–186; (b) Dorwald, F. Z. *Metal Carbenes in Organic Synthesis*; Wiley-VCH, Verlag GmbH: Weinheim, 1999; (c) Herndon, J. W. *Coord. Chem. Rev.* **2000**, *206–207*, 237.

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

13. Hegedus, L. S.; McGuire, M. A.; Schultze, L. M. *Org. Synth.* **1987**, *65*, 140.

14. Schwindt, M. A.; Lejon, T.; Hegedus, L. S. *Organometallics* **1990**, *9*, 2814.

15. Fayos, J.; Clardy, J.; Dolby, L. J.; Farnham, T. *J. Org. Chem.* **1977**, *42*, 1349.

16. Casey, Ch. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1976**, *118*, 309.