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Aminocarbene Complexes of Chromium and Molybdenum: Initiators for Cascade Reactions with Alkynes Leading to New Heterocyclic Compounds *via* Nitrogen Ylides

By H. Rudler, M. Audouin, E. Chelain, B. Denise, R. Goumont, A. Massoud, A. Parlier, A. Pacreau, M. Rudler, R. Yefsah, C. Alvarez, and F. Delgado-Reyes
LABORATOIRE DE CHIMIE ORGANIQUE, URA 408, UNIVERSITÉ PIERRE ET MARIE CURIE T44, 4 PLACE JUSSIEU, 75252 PARIS CEDEX 05

1 Introduction

Since the discovery of the first carbene complexes of transition metals by Fischer in 1964[1] the chemistry of this type of compound has moved gradually on from the more fundamental and structurally oriented aspect, until now the possibility exists of using these complexes as versatile synthons in organic synthesis.[2–5]

The parallel between the olefin metathesis and cyclopropanation reactions and the interaction of carbene complexes with olefins led to the synthesis of model compounds, essentially derived from Fischer carbene complexes, which mimic this type of reaction.[6–10] A second important development arose from the idea that just as olefins can cycloadd to carbene complexes to give metallacyclobutanes followed by new olefins and new carbene complexes, so alkynes might cycloadd to Fischer carbene complexes providing first metallacyclobutenes, then new non-heteroatom-stabilized carbene complexes, namely vinylidene carbene complexes. This proved to be a fruitful approach—the pioneering developments were mainly by Dötz[11,12]—and it was later also applied to the polymerization of alkynes.[13,14] The key step in these reactions is the formation, after alkyne insertion, of an elusive but highly reactive carbene complex able to promote, under precise conditions, interesting transformations; the first example uncovered was the interaction with aromatics and CO, known as the benzannulation reaction. This reaction leads, as shown in Scheme 1, to phenolic compounds, and has been used

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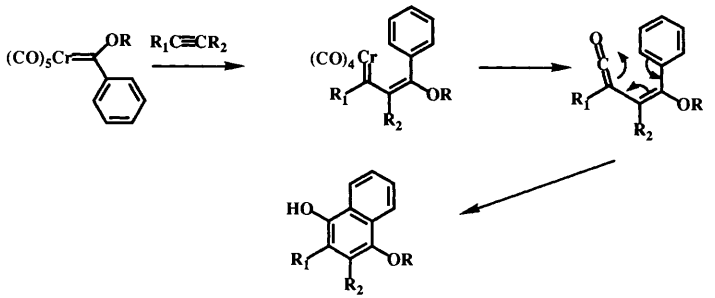
[2] K H Dotz, H Fischer, P Hofmann, F R Kreissl, U Schubert, and K Weiss, 'Transition Metal Carbene Complexes', Verlag Chemie, Deerfield Beach, F L, 1984
[3] U Schubert, 'Advances in Metal Carbene Chemistry', Kluwer Acad Publishers, Dordrecht, 1989
[4] J A Connor, *Topics Current Chem*, 1977, **71**, 71
[5] E O Fischer and R Aumann, *Angew Chem*, 1967, **79**, 191
[6] C P Casey, N W Vollendorf, and K J Haller, *J Am Chem Soc*, 1984, **106**, 3754
[7] C P Casey and A J Shusterman, *Organometallics*, 1985, **4**, 736
[8] C Alvarez, H Rudler, J C Daran, and Y Jeannin, *J Chem Soc Chem Commun*, 1984, 547
[9] C P Casey, N L Hornung, and W P Kosar, *J Am Chem Soc*, 1987, **109**, 4908
[10] D J Cardin, M J Doyle, and M F Lappert, *J Chem Soc Chem Commun*, 1972, 927
[11] K H Dotz, *Angew Chem Int Ed Engl*, 1975, **14**, 644
[12] K H Dotz, *Angew Chem Int Ed Engl*, 1984, **23**, 587
[13] T J Katz, J McGinnis, and C Altus, *J Am Chem Soc*, 1976, **98**, 606
[14] D J Liaw, A Soum, M Fontanille, A Parlier, and H Rudler, *Makromol Chem Rapid Commun*, 1985, **6**, 309



Scheme 1

widely since 1974, and applied by several groups successfully to the synthesis of polycyclic compounds such as vitamins, antibiotics, *etc.*

At this point a few comments are in order: First, most of the insertion reactions were carried out on alkoxycarbene complexes of chromium since the tungsten analogues were known to be much more stable (CO groups less labile).[4] Secondly, no attempts to use this approach for the intramolecular cyclopropanation of simple olefins had been described; this was probably due to the fact that Fischer carbene complexes only sluggishly transferred their carbene moiety to double bonds.[2] Thirdly, although aminocarbene complexes had been known from the beginning[5] (and, according to Fischer, were very easy to synthesize and to handle) no attempts had been made, to the best of our knowledge, to use this type of complex as a nitrogen-containing synthon with alkynes (at least until 1984).

There existed therefore a gap in the chemistry of Fischer carbene complexes that we were prompted to fill, since it bore directly on our previous work on alkene–carbene complexes of tungsten and chromium.[15] Thus, most of the chemistry on aminocarbene complexes has been disclosed very recently[16]—much of it (as far as the thermal cycloadditions are concerned) from our laboratory.[17–23] These complexes are now being used actively by several other groups, both in photochemical[24] and thermal[25–29] cycloaddition reactions.

The purpose of this account is to describe our results in the field of thermal insertion of alkynes into aminocarbene complexes of tungsten, chromium, and molybdenum. We will briefly describe work on the intramolecular cyclopropana-

[15] A. Parlier, H. Rudler, N. Platzer, M. Fontanille, and A. Soum, *J. Organomet. Chem.*, 1985, **287**, C-8.
[16] A. Yamashita, *Tetrahedron Lett.*, 1986, 5915.
[17] A. Parlier, H. Rudler, and R. Yefsah, *J. Organomet. Chem.*, 1987, **328**, C-21.
[18] A. Parlier, H. Rudler, R. Yefsah, J. C. Daran, and C. Knobler, *J. Chem. Soc., Chem. Commun.*, 1988, 635.
[19] B. Denise, A. Parlier, H. Rudler, J. Vaissermann, and J. C. Daran, *J. Chem. Soc., Chem. Commun.*, 1988, 1303.
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[21] C. Alvarez, A. Parlier, H. Rudler, R. Yefsah, J. C. Daran, and C. Knobler, *Organometallics*, 1989, **8**, 2253.
[22] M. Audouin, S. Blandiniere, A. Parlier, and H. Rudler, *J. Chem. Soc., Chem. Commun.*, 1990, 23.
[23] B. Denise, A. Parlier, R. Goumont, J. Vaissermann, J. C. Daran, and H. Rudler, *J. Chem. Soc., Chem. Commun.*, 1990, 1138.
[24] C. Borel, L. S. Hegedus, J. Krebs, and Y. Satoh, *J. Am. Chem. Soc.*, 1987, **109**, 1101.

tion reaction and show that the most significant and innovative aspects of this chemistry are related to the formation and rearrangement of nitrogen ylides.

2 Synthesis and Structure of Alkene–Aminocarbene Complexes

A. Introduction.—The synthesis and study of the reactivity of aminocarbene complexes of tungsten, chromium, and molybdenum were part of a general project—the low-temperature interaction (at or below room temperature) of alkynes with Fischer carbene complexes. This problem was solved by the synthesis of a complex bearing a strained bidentate alkene–carbene ligand which underwent fast decoordination of the double bond, thus allowing easy insertion of alkynes into the carbene function. μ-Carbene complexes of tungsten[30] bearing a coordinated carbon–carbon double bond were shown to insert alkynes stepwise, at room temperature (Scheme 2).

Thus complexes (2), obtained from (1), react *at room temperature* with alkynes to give (3) after insertion of the alkyne, and then by an intramolecular cyclopropanation reaction give bicycloheptane derivatives (4) (Scheme 3).[15,31]

Four points are worthy of note: First, when the double bond is not coordinated to the metal as in (1), no reaction is observed *at room temperature*.[31] Secondly, ligands, such as PPh_3, easily de-coordinate the double bond.[32] Thirdly, the intramolecular cyclopropanation takes place under the best conditions when the double bond, whether in an alkyl chain or in a ring, is in the γ position with respect to the carbene function.[31] Finally, no CO insertion reaction is observed.

On paper a logical approach to azabicycloheptane derivatives (6) would therefore be the interaction of alkynes with complexes of type (5) (Scheme 4).

B. Synthesis and Structure of Bidentate Alkene–Aminocarbene Complexes.—Aminocarbene complexes had initially been prepared by Fischer by substitution of the alkoxy group by ammonia or amines (Scheme 5).[5] This reaction is limited to primary and a few secondary amines, especially cycloamines. More recent methods, with broader application, have been described by Lappert[33] and by Hegedus:[24] reaction of $Na_2Cr(CO)_5$ with Vilsmeier salts or amides, followed by dehydration, leads to various aminocarbene complexes, among which are the interesting complexes bearing a hydrogen on the carbene carbon (Scheme 6).

A peculiar observation with aminocarbene complexes is the existence, as a result of extensive π-bonding between the carbene carbon and the nitrogen atom, of *E*/*Z* isomers isolable at room temperature, the thermal isomerization of which takes place only at elevated temperature (*i.e.* boiling toluene). As a consequence, a reinforcement of the bonding of the CO groups to the metal is observed: thus, substitution of the CO groups by external ligands is more difficult, a corollary of this being a lower reactivity of the carbene function.[5]

[25] L. S. Hegedus and D. B. Miller, Jr., *J. Org. Chem.*, 1989, **54**, 1249.
[26] K. H. Dötz, H. G. Erben, and K. Harms, *J. Chem. Soc., Chem. Commun.*, 1989, 692.
[27] K. H. Dötz, T. Schäfer, and K. Harms, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 176.
[28] R. Aumann and P. Hinterding, *Chem. Ber.*, 1990, **123**, 611.
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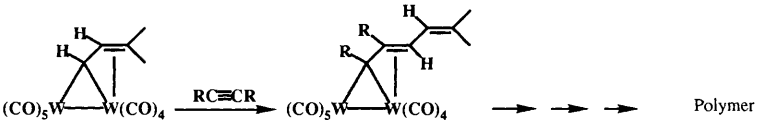
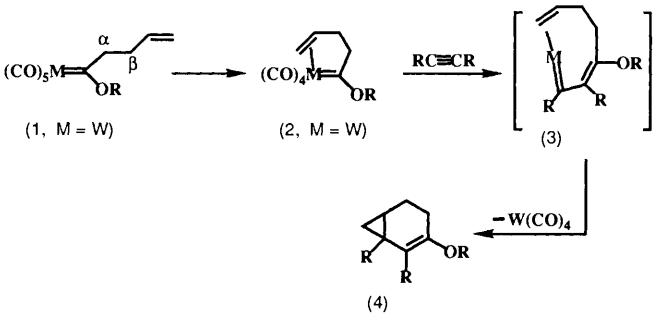
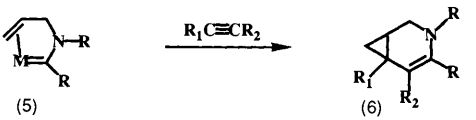


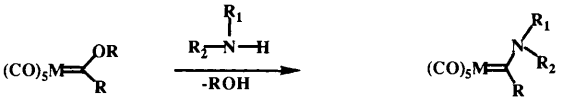
Scheme 2



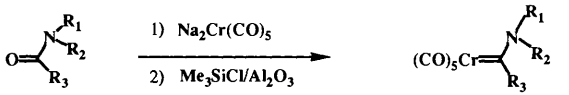
Scheme 3



Scheme 4



Scheme 5



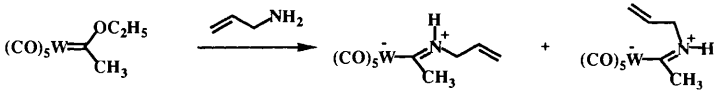
Scheme 6

Alkene–aminocarbene complexes of tungsten had already been described and thoroughly studied by Casey,[34] and alkene–aminocarbene complexes of molybdenum had been prepared by Lappert and were known to undergo an easy

[30] J Levisalles, F Rose-Munch, H Rudler, J C Daran, Y Dromzee, and Y Jeannin, *J Chem Soc Chem Commun*, 1981, 152
[31] A Parlier, H Rudler, N Platzer, M Fontanille, and A Soum, *J Chem Soc Dalton Trans*, 1987, 1041
[32] C Alvarez, A Pacreau, A Parlier, H Rudler, and J C Daran, *Organometallics*, 1987, **6**, 1057
[33] A J Hartshorn, M F Lappert, and K Turner, *J Chem Soc Dalton Trans*, 1978, 348
[34] C P Casey and A J Shusterman, *J Mol Cat*, 1980, **8**, 1

(5) (7)

Scheme 7



(8) (9*E*, 85%) (9*Z*, 15%)

Scheme 8

aza-Claisen rearrangement.[3,35]

1,5-Bidentate aminocarbene complexes of tungsten had been used as models for the intramolecular cyclopropanation reaction of alkenes; like the 1,5-alkenyl–alkoxycarbene complexes of tungsten, prepared in this laboratory, they underwent an easy intramolecular cyclopropanation reaction upon heating.[6–8] We therefore felt that, like 1,4-bidentate alkene–alkoxycarbene complexes, 1,4-bidentate aminocarbene complexes also might undergo alkyne insertion–cyclopropanation reactions, perhaps under more drastic conditions.

In order to check the influence of nitrogen on the alkyne insertion reaction, we synthesized complexes of structures (5) and (7) (Scheme 7).[36] Since we expected a lower reactivity for aminocarbene complexes, and since, in general, chromium carbene complexes are known to be more reactive than tungsten carbene complexes (M–CO weaker for M = Cr than for M = W), we synthesized both type of complexes using the sequences indicated above. In the case of (9) the *E* and *Z* isomers could be separated by chemical means (Scheme 8), and therefore, for the first time, two isomers around the C–N double bond, bearing a free carbon–carbon double bond, could be fully characterized by *X*-ray spectroscopy (Figures 1 and 2).[37]

A difference of reactivity in going from Cr to W became apparent during the double bond coordination reactions: whereas the coordination of the *Z* double bonds of Cr complexes took place at room temperature (best conditions, refluxing hexane), the coordination of the *Z* double bonds of W complexes needed refluxing benzene.[36]

3 Reaction of Alkene–Aminocarbene Complexes with Alkynes

A. Insertion–Cyclopropanation for the *Z*-isomers.—One of the striking points with either μ-carbene or 1,4-bidentate alkene–carbene complexes of tungsten and chromium was their high reactivity towards alkynes, even at room temperature.

[35] J. A. Chamizo and M. F. Lappert, *J. Org. Chem.*, 1989, **54**, 4684.
[36] A. Parlier, H. Rudler, J. C. Daran, C Alvarez, and F. Delgado-Reyes, *J. Organomet. Chem.*, 1987, **337**, 339.
[37] A. Parlier, H. Rudler, J. C. Daran, and C. Alvarez, *J. Organomet. Chem.*, 1987, **333**, 245

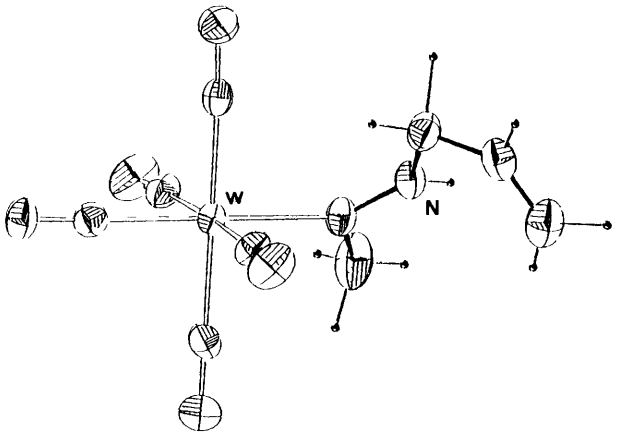


Figure 1

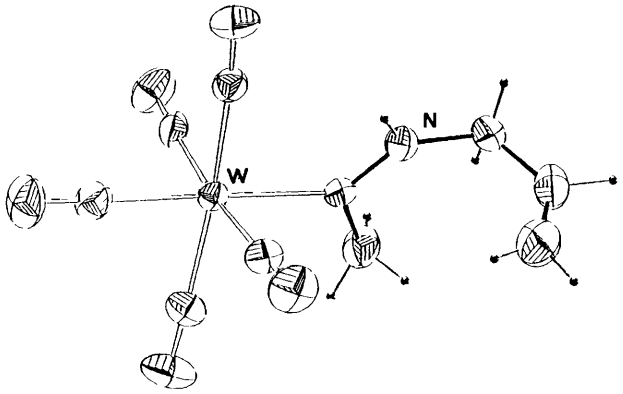
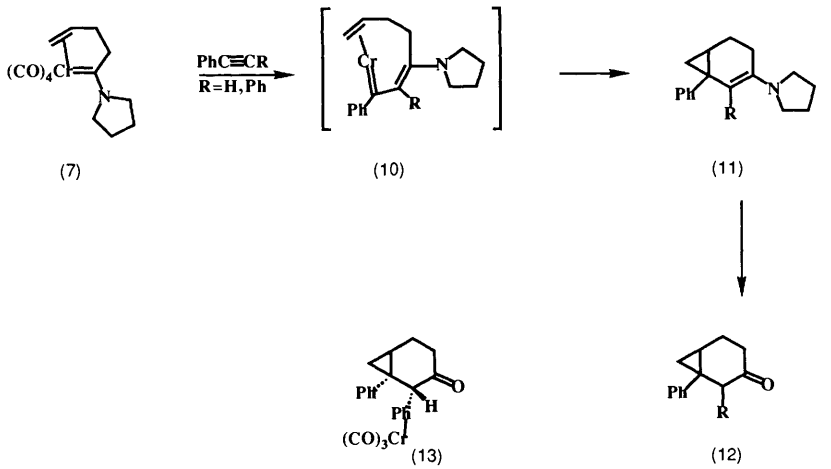


Figure 2

There was, however, a difference of reactivity between bidentate alkene–alkoxycarbene complexes and bidentate alkene–aminocarbene complexes. Although the latter complexes contain the same strained cycle, the presence of nitrogen makes the substitution reaction much more difficult: thus no reaction took place, *at room temperature*, between phosphines or alkynes and these aminocarbene complexes. The tungsten aminocarbene complexes were even reluctant to react in refluxing benzene or toluene. However, the chromium complexes reacted smoothly with alkynes in refluxing benzene. For example, complex (7) reacted with phenyl and diphenylacetylene to give (after silica gel chromatography) the expected and already described ketones (12) *via* their enamines (11) (Scheme 9). In the case where R = Ph, the ketone was obtained as the $Cr(CO)_3$ complex (13), and thus, for the first time, the structure of these



Scheme 9

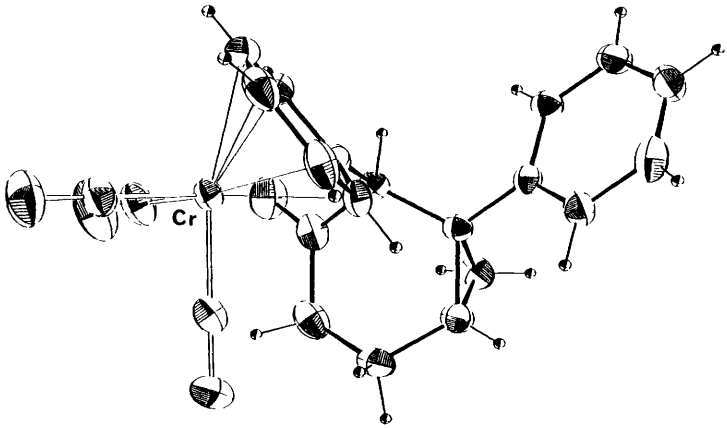
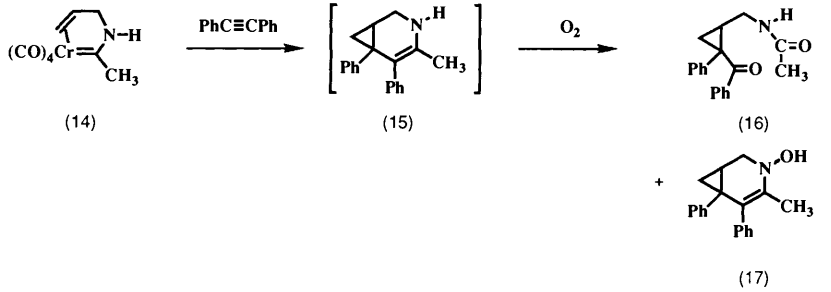


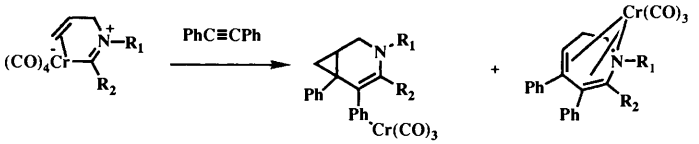
Figure 3

bicycloheptane derivatives could be ascertained by a single crystal *X*-ray analysis (Figure 3).[38]

Conversely, when the nitrogen atom was in the coordinated chain, as in (14) and (18)—(21), nitrogen-containing heterocycles resulted. Several structures were obtained in these cases and the results were highly dependent on the substituent on nitrogen. However, in all cases so far examined, the alkyne insertion took place *without CO insertion.* For example, when complex (14) was caused to react with diphenylacetylene (or other alkynes), the expected azabicycloheptane (15) was not obtained. Instead, after work-up and chromatography, the oxidative



Scheme 10



(18; $R_1 = CH_3$, $R_2 = CH_3$)	(22) 51%	(23) 0%
(19; $R_1 = CH_2Ph$, $R_2 = CH_3$)	24%	12%
(20; $R_1 = CH_2CH{=}CH_2$, $R_2 = CH_3$)	18%	9%
(21; $R_1 = CH_3$, $R_2 = H$)	70%	0%

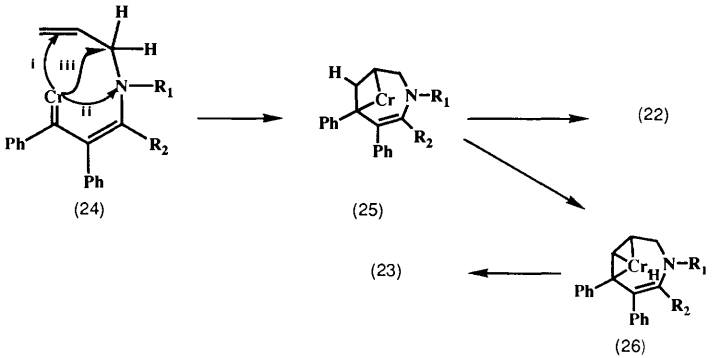
Scheme 11

double bond cleavage product (16) was obtained in 55% yield, along with minor amounts of the two isomers of the *N*-hydroxy enamines (17) (10%). Thus, the expected enamine (15) had been oxidized during work-up: this result is not surprising since it is known that this type of enamine readily suffers double bond cleavage by oxygen to give ketoamides (Scheme 10).[17] The expected complexes (22) were however obtained when R ≠ H.[21]

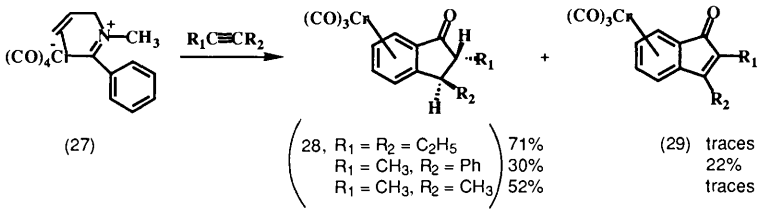
The course of the reaction was again somewhat unexpected when different substituents were introduced on nitrogen. Thus in the cases where R = benzyl or allyl, besides (22), dihydroazepine complexes (23) were obtained (12 and 9%) (Scheme 11). Heating (22) (R = benzyl or allyl) in either the absence or the presence of $Cr(CO)_6$, in boiling benzene, did not lead to (23): thus (23) is not a rearrangement product of (22).[39,40]

The new carbene complex (24), formed upon alkyne insertion (Scheme 12), has the choice of three targets: the double bond (i), the nitrogen atom (ii), or the C–H bond in the α position with respect to nitrogen (iii). However, only the coordinated double bond seems to be involved: the cyclopropanes are the result of a classical intramolecular reaction, and the dihydroazepines (23) the result

[38] Unpublished results.
[39] B. Denise, R. Goumont, A. Parlier, H. Rudler, J. C. Daran, and J. Vaissermann, *J. Organomet. Chem.*, 1989, **377**, 89.
[40] A. Parlier, R. Yefsah, M. Rudler, H. Rudler, J. C. Daran, and J. Vaissermann, *J. Organomet. Chem.*, 1990, **381**, 191.



Scheme 12

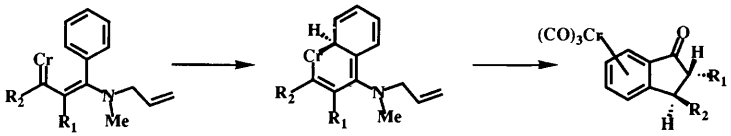


Scheme 13

from a formal point of view, of a direct insertion into the terminal vinylic hydrogen.

It is likely that both (22) and (23) arise from the rearrangement of a common intermediate, a chromacyclobutane (25), which can undergo either a reductive elimination to form a cyclopropane, or a β-elimination, *via* (26) to the ring-opened derivative (23).[40]

(i) *The Influence of an Aryl Group on the Carbene-carbon: Benzannulation Reaction without CO Insertion.*—Carbene complexes bearing a phenyl group on the carbene-carbon generally lead to benzannulation products (Scheme 1) as the result of both the alkyne and CO insertions.[11,12] The presence of a coordinated double bond in complexes (27) might, however, hinder the interaction of the aromatic group with the new carbene complex formed upon alkyne insertion. This has not been found to be the case. In all examples studied so far, only products due to the annulation have been obtained. However, an important difference did appear: *no CO insertion took place.* The sole products isolated were complexes (28) and (29) of, respectively, indanones and indenones (Scheme 13).[21] This result is important from a mechanistic point of view: it means first that de-coordination of the double bond takes place, and secondly—a point which had not been settled—that prior to CO insertion, carbene complexes of chromium, like those of rhodium,[41] do interact with aromatic rings.



Scheme 14

A last point which deserves comment is the *cis* relationship of R^2 with respect to $Cr(CO)_3$ which indicates that a 1,5-sigmatropic hydrogen shift took place during the re-aromatization reaction (Scheme 14). A similar result has been obtained by Dötz and co-workers.[26]

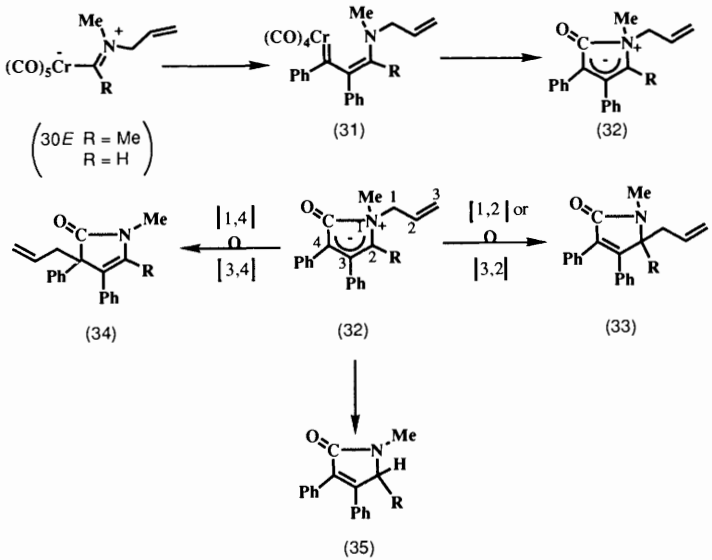
B. Formation and Rearrangement of N-Ylides for the *E*-Isomers: A New Cascade Reaction.—Our observation that like alkene–alkoxycarbene complexes, aminocarbene complexes of the same structure underwent the alkyne insertion reaction rekindled our interest in this type of complex. Since we could separate cleanly a mixture of *E*/*Z* isomers by selectively coordinating the double bond of one of the two isomers (simple heating in hexane),[37] we were able to carry out the insertion separately on the two isomers, or better on the bidentate alkene–aminocarbene complex and on the *E* isomer. Fast isomerization was not expected to take place under the insertion reaction conditions and thus we were confident of seeing a different behaviour for the *E* isomer in the insertion reaction. Indeed, a *trans* orientation of the double bond might preclude its interaction with the metal, and thus with the carbene function. The sole remaining targets for the carbene function in (31) would then be nitrogen. And this was indeed confirmed.

After reaction of complex (30) with diphenylacetylene in boiling benzene, pyrrolinones (33), (34), and (35), the latter in trace amounts, were isolated and fully characterized.[40]

The two main products of the reaction are the result of the alkyne and CO insertions into (30) together with a migration of the allyl group from nitrogen either to C-2, the carbene-carbon, or to C-4, a carbon of the inserted alkyne: such migrations are reminiscent of the rearrangement of N-ylides, which occurs in the Stevens rearrangement.[42–47] Structures which might account for such rearrangements in the present case are given in Scheme 15.

Thus, from a formal point of view, (33) can be considered as the result of the rearrangement of the N-ylide (32), the timing of the different steps leading to (32) (alkyne insertion, CO insertion, ylide formation) being unspecified at this point.

[41] G Maas, *Topics Current Chem*, 1987, **137**, 75 and references cited therein
[42] T S Stevens, E M Creighton, A B Gordon, and M McNicol, *J Chem Soc*, 1928, 3193
[43] T Thomson and T S Stevens, *J Chem Soc*, 1932, 55
[44] S H Pine, 'Organic Reactions', Vol 18, Wiley, 1970, p 403
[45] M Sivapathasuntharam, W D Ollis, and I O Sutherland, *J Chem Soc*, *Perkin Trans 1*, 1981, 1953
[46] W D Ollis, M Rey, and I O Sutherland, *J Chem Soc Perkin Trans 1*, 1983, 1009
[47] K Chantrapromma, W D Ollis, and I O Sutherland, *J Chem Soc*, *Perkin Trans 1*, 1983, 1049 and references therein



Scheme 15

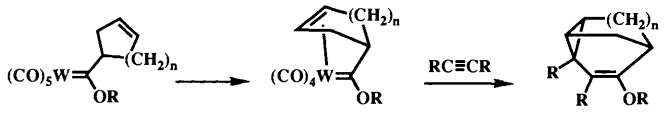
At first glance, the formation of (33) and (34) could be explained in terms of, respectively, a (3,2) or a (3,4) sigmatropic rearrangement of ylide (32). Since, however, no substituent is present on the double bond of the allyl group, it is not possible to eliminate the (1,2) or (1,4) migrations.

As for (35), its formation can be explained in the same way except that during the rearrangement of (32) loss of the allyl group must occur. Such a reaction is also typical of the Stevens rearrangement of chemically produced N-allyl ylides: it is in this case an indication of the involvement of radicals.

However, examination of the following examples (Scheme 15) provided some clues to the involvement of both concerted and non-concerted rearrangements.

C. Formation and Rearrangement of N-Ylides from Unsaturated Cycloamines: Ring Expansion and Contraction Reactions upon (1,2) **and** (3,2) **Migrations.**—The involvement of other mechanisms, especially the (1,2) rearrangement of allylic groups, could be demonstrated when complexes (42) and (48) were submitted to the alkyne insertion reaction.

Keeping in mind that complexes (36; n = 1,2) underwent the double bond coordination reaction to give (37), and furthermore that (37) reacted with alkynes to give the interesting polycyclic ethers (38) (Scheme 16),[31] we synthesized complexes (42) and (48). Whereas complexes (48) exist as single isomers, complexes (42; R = CH_3, Ph, H) exist as pairs of isomers. Moreover the single crystal *X*-ray structure (Figure 4) of (48) clearly shows that, due to its dipolar nature, the whole carbene ligand is planar, with the double bond far away from



(36; n = 1, 2) (37) (38)

Scheme 16

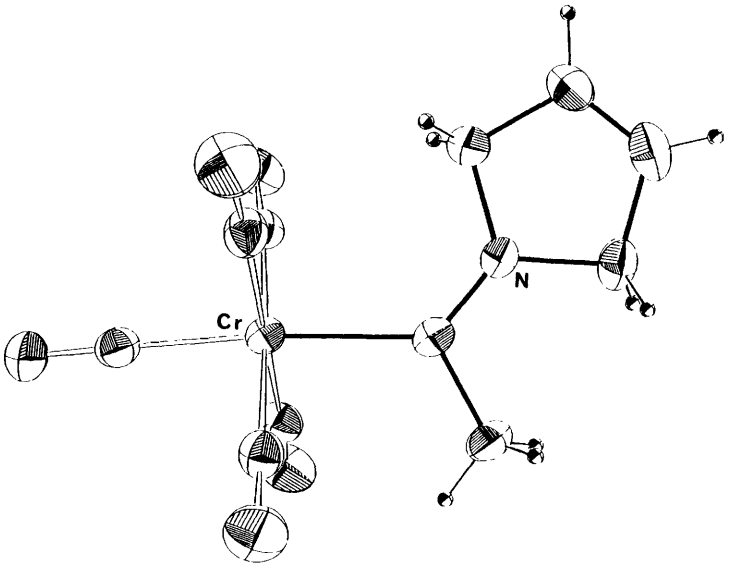
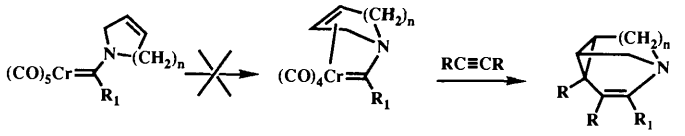


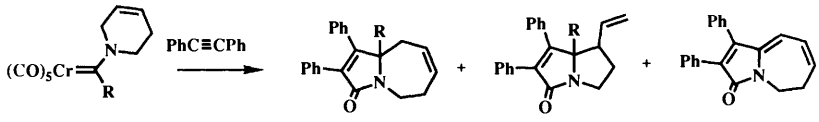
Figure 4



(39) (40) (41)

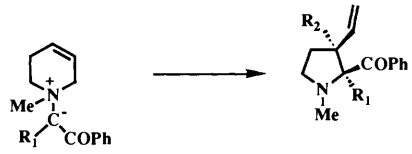
Scheme 17

the metal.[20] Thus, the planned series of experiments (39) ⟶ (40) ⟶ (41) appeared to be difficult to realize. And indeed, the first step, the coordination of the double bond of both (42) and (48), did not occur, even under drastic conditions (Scheme 17).[3,20] We were therefore in the same situation as for (30*E*): the double bond is not an obvious target for the carbene formed upon insertion of an alkyne. And indeed the reaction of complexes (42; R = CH_3) and (48) occurred as for (30*E*). For example (42) gave a mixture of (43) and (44) (Scheme 18). The most abundant product, (44), is the result of the same series of discrete reactions as for the transformation of (30*E*) into (33), but in this case the (3,2)



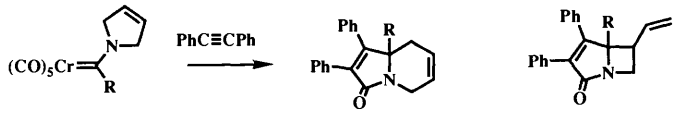
(42, R = H, CH_3, Ph) (43) (44) (45)

Scheme 18



(46) (47)

Scheme 19



(48, R = CH_3, Ph, cyclopropyl) (49) (50)

Scheme 20

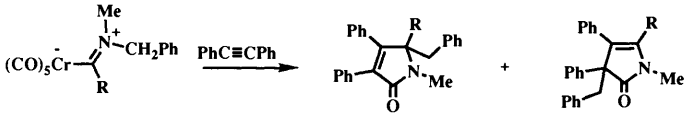
sigmatropic rearrangement could account for the ring contraction, with formation of an exocyclic vinyl group. This transformation can again be compared to the Stevens rearrangement of the structurally related N-ylide (46) which leads to the sole product (47) by (3,2) sigmatropic rearrangement (Scheme 19).[45] However, in the case of (42) the (1,2) migration operates also, since the ring expansion product (43) is also observed.[19,20]

In the case where R = H, two additional compounds (45) and (41) were isolated in low yield (5%); (45) was the product of the dehydrogenation of (43; R = H), and (41) the result of the expected intramolecular cyclopropanation reaction of the tetrahydropyridine double bond.[38] No benzannulation reaction was observed with (42; R = Ph).[20] This result probably implies that in the intermediate which is formed upon the alkyne insertion, the nitrogen atom stays close to the metal, a situation which hinders the interaction of the phenyl group with the carbene function.

With the five-membered pyrrolino-substituted carbene complexes (48) only compounds (49), the products of the (1,2) rearrangement, were obtained; no products due to the allowed (3,2) sigmatropic rearrangement, the lactam (50), could be detected (Scheme 20). Again no benzannulation reaction occurred with (48; R = Ph).[20]

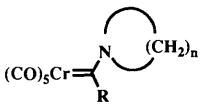
4 Formation and Rearrangement of N-Ylides Bearing Groups Different from the Allyl Group

It is known that in N-ylides, groups other than allylic groups are able to migrate.



(51; R = CH_3, H) (52) (53)

Scheme 21



(54; R = H, CH_3, Ph, cyclopropyl, thienyl
n = 2, 3, 4, 5, 6, 7)

Scheme 22

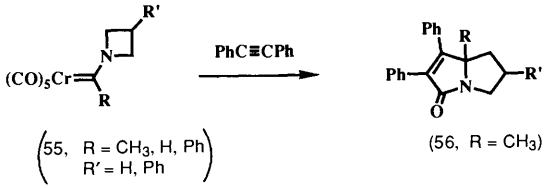
In these cases, the involvement of radicals has been demonstrated. Since in the examples already described, products arising from non-concerted rearrangements were observed, it is highly probable that at least part, if not all, of the rearrangement reactions take place by some other mechanisms.

A. Benzyl-substituted Aminocarbene Complexes: Formation of Pyrrolinones.— One of the functions which migrates the most easily (because of the formation of stable radicals) from nitrogen to carbon in N-ylides is the benzyl group.[42,43] We therefore studied the reactivity of complexes (51; R = H, CH_3) towards alkynes. With (51; R = H), only pyrrolinone (53) (R = H) was isolated (in 40% yield), whereas both (52) and (53) were obtained with (51; R = CH_3). Thus (51) behaves like the allyl-substituted aminocarbene, *viz.* alkyne/CO insertions along with nitrogen to carbon migration of the benzyl group take place (Scheme 21).[39]

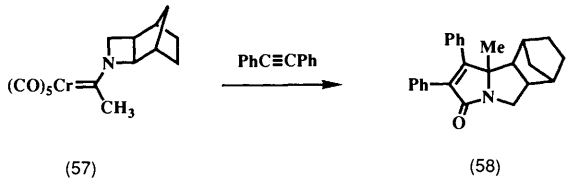
Since the reactivity of the carbene complexes, and especially of the N-ylide intermediates, appeared to parallel the behaviour of N-ylides in general, extension of these insertion–rearrangement reactions to other cycloaminocarbene complexes looked promising, especially as far as the application to organic synthesis was concerned. Thus a series of complexes of the type (54; R = H, CH_3, Ph) were prepared in order to check their reactivity (Scheme 22).

B. Azetidinocarbene Complexes: Synthesis of Pyrrolizidine Derivatives.— Azetidinocarbene complexes might be interesting starting materials for the synthesis of pyrrolizidine derivatives bearing various groups at the ring junction, provided that the ring expansion takes place. The synthesis of complexes (55) was straightforward by both methods. Complex (55; R = CH_3) gave, upon heating with PhC≡CPh, the expected pyrrolizidine derivative (56) in 52% yield. A second azetidinocarbene complex (57) behaved similarly: it led, upon insertion–rearrangement, to the tetracyclic compound (58; 45%) (Schemes 23 and 24).[48]

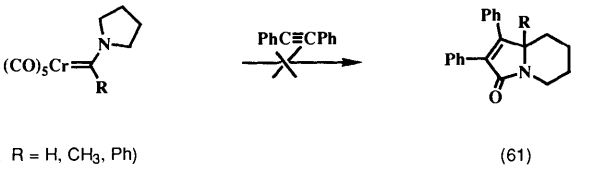
[48] A. Massoud, PhD Thesis, P. M. Curie University, Paris, 1991.



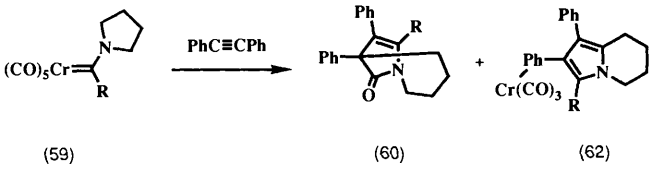
Scheme 23



Scheme 24



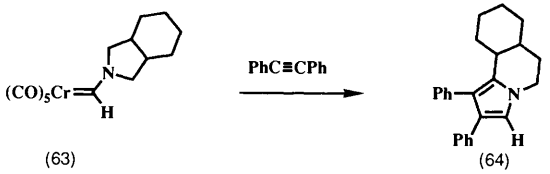
Scheme 25



Scheme 26

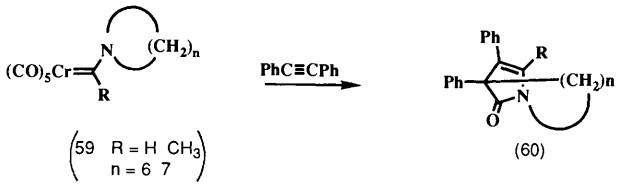
C. Aminocarbene Complexes Bearing Larger Ring Systems: Synthesis of Bridgehead Bicyclic Lactams.—It is known that like N-ylides derived from quaternary ammonium salts of azetidine those derived from five-membered heterocycles can (although with more difficulty) undergo ring-expansion reactions. Since in the case of the pyrroline-substituted carbene complexes only the ring-expansion products were obtained [by a (1,2) migration[20]], we expected to obtain (61) from (59) (Scheme 25). However, these carbene complexes appeared to be more stable than the complexes described up to now, and led to more complex mixtures of products.

Thus (59; n = 4, R = H, CH_3, Ph) gave only trace amounts of (61); the major product was (60), a bridgehead bicyclic amide (Scheme 26), in respectively 35% (R = H), 32% (R = CH_3), and 58% (R = Ph) yield. These products are the result of the (1,4) migration of a N–C bond. Again noteworthy is the reaction with (59; R = Ph) where no benzannulation reaction could be detected.[20]



(63) (64)

Scheme 27



(59 R = H CH_3; n = 6 7) (60)

Scheme 28

However, besides products of structure (60), substituted pyrroles (62) were isolated in 22% (R = CH_3) and 15% (R = H) yield Starting with complex (63) the pyrrole (64), which was fully characterized by an *X*-ray analysis, was the main product of the reaction (Scheme 27) [23]

From a formal point of view these pyrroles are the result of both the alkyne/CO insertion reactions and of the deoxygenation of the intermediate ketene, followed by a nitrogen to carbon migration of an alkyl group Although the deoxygenation of ketene complexes is known to lead to vinylidene carbene complexes,[49] another mechanism must be considered here (*vide infra*)

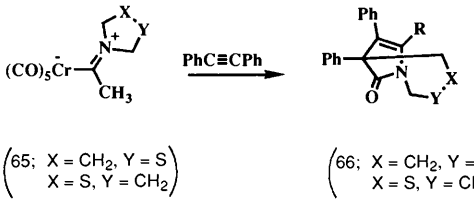
With the exception of the six-membered ring system, with which we will deal later on, larger ring systems showed the same behaviour in the insertion reaction the examples so far examined have given products of the general structure (60), bridgehead bicyclic lactams, in yields of 40% for $n = 6$, R = H and 25% for $n = 7$, R = CH_3 (Scheme 28) However, in these latter cases no pyrroles were detected

Introduction of a second heteroatom into the five-membered ring system (*e g* thiazolidine) did not modify the course of the insertion reaction, both isomers of (65) reacted with diphenylacetylene to give (though in low yield) the isomeric bridgehead thiolactams (66) (Scheme 29) [38]

5 Aminocarbene Complexes Bearing Substituents on Nitrogen of Low Migratory Aptitude: Formation of Stable Nitrogen Ylides

In the examples of alkyne-insertion/rearrangement reactions examined up to now, it seems that, in general, the reactions observed parallel most aspects of the Stevens rearrangement of N-ylides However, the reaction of the chromium

[49] G L Geoffroy and S L Bassner in Advances in Organometallic Chemistry Academic Press 1988 Vol 28 p 1

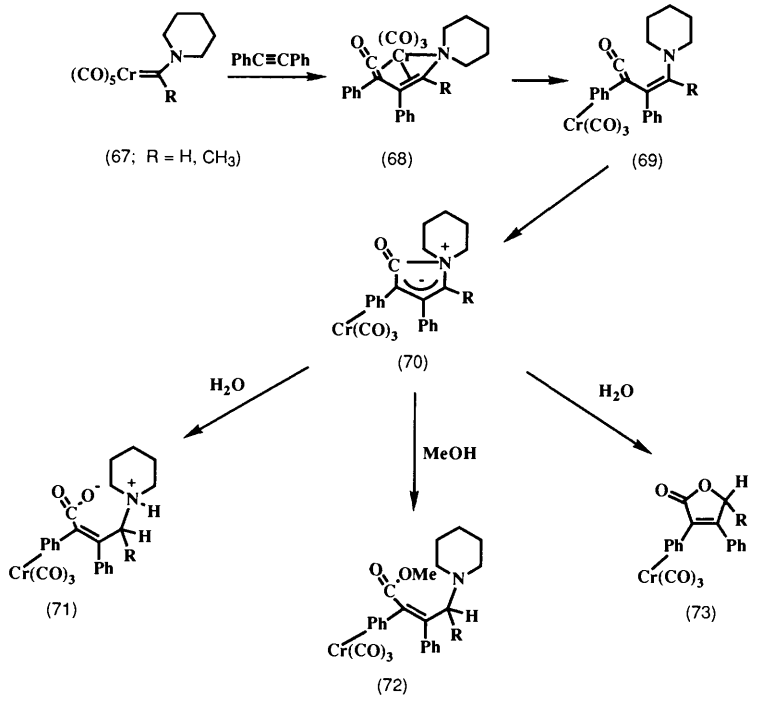


Scheme 29

carbene complexes is more complicated. Indeed, additional steps are observed. For instance, before the ylide rearrangement can take place, a new carbene must be formed, although the starting complex already has a dipolar structure. Moreover, at some stage of the reaction, CO insertion must take place. A mechanistic point, the timing of the different steps, required to be settled. The question was therefore to establish whether it would be possible to stop the reaction at some point. For that purpose we chose to study the reactivity of aminocarbene complexes bearing groups of known low migratory aptitude in the Stevens rearrangement of N-ylides, such as alkyl groups or a six-membered ring system. We expected to observe at least the alkyne insertion reaction and perhaps the CO insertion reaction. And this was indeed the case for several examples where we could observe 'incomplete' reactions; the most thoroughly studied complexes were (67) and (74) (Scheme 30).[23,50] For example, (67; R = H) reacted with PhC≡CPh in cyclohexane to give complex (70; R = H, 60%) which precipitated as a yellow powder. Upon recrystallization, partial hydrolysis to the amino-acid (71) took place. The structure of (71), confirmed by a single crystal *X*-ray analysis, showed that a shift of $Cr(CO)_3$ took place. When the same reaction was conducted in moist benzene the unsaturated lactone (73), resulting from the complete hydrolysis of the intermediate, was formed along with (71) (Scheme 30).[23]

Both results were consistent with a structure such as (69), an enaminoketene. However, the spectroscopic data did not agree with such a structure. Both the infra-red (ν CO, 1700 cm^{-1}) and the ^{13}C NMR spectra (δ CO, 169 ppm) rather indicated the existence of a through-space interaction between the nitrogen atom and the ketene function. A structure such as (70), a nitrogen ylide, was therefore more likely. And this was finally demonstrated by carrying out an *X*-ray analysis on the moisture-sensitive crystals of (70).[50] The geometry of this important intermediate appears in Figure 5 and features a non-linear ketene function associated with a tetrahedric nitrogen centre at a rather long distance from each other (1.56 Å). As a consequence, the most labile bond in (70) is C(O)–N: thus hydrolysis leads logically to (71) whereas methanolysis instantaneously gives the corresponding aminoester (72) (Scheme 30).[23] Under the same conditions complex (74) gave the ylide complex (75) (Scheme 31).

[50] H. Rudler, A. Parlier, R. Goumont, J. C. Daran, and J. Vaissermann, *J. Chem. Soc., Chem. Commun*, 1991, 1075.



Scheme 30

It is interesting to note at this point that the same type of ylide intermediates could also be observed during the intramolecular reaction carried out on the aminocarbene complexes (76) (Scheme 32). Upon heating in cyclohexane, these complexes gave the moisture-sensitive ylides (78) as yellow crystals *via* the ketene complexes (77), which could both be characterized by *X*-ray analysis (Figures 6 and 7).[51]

However, slight modifications in the structure of the starting complex deeply modified the course of the reaction. Thus complex (79) gave under the same conditions ketone (82), the product arising from the sole alkyne insertion, *via* (80) and (81) (Scheme 33); complex (83) led to the organic compound (85) (40% yield) upon alkyne/CO insertion and a N–CH activation reaction (Scheme 34).[22]

Finally, support for the general involvement of ylides came also from the observation of the reactivity of thiocarbene complexes. For example complex (86) led, in the presence of PhC≡CPh, to a mixture of thiolactones (87) and (88) as a result of, respectively, allyl migration from sulphur to carbon and loss of the allyl group, probably *via* sulphur ylide intermediate (Scheme 35).[52]

[51] E. Chelain, A. Parlier, H. Rudler, J. C. Daran, and J. Vaissermann, *J. Organomet. Chem.*, 1991, in press.

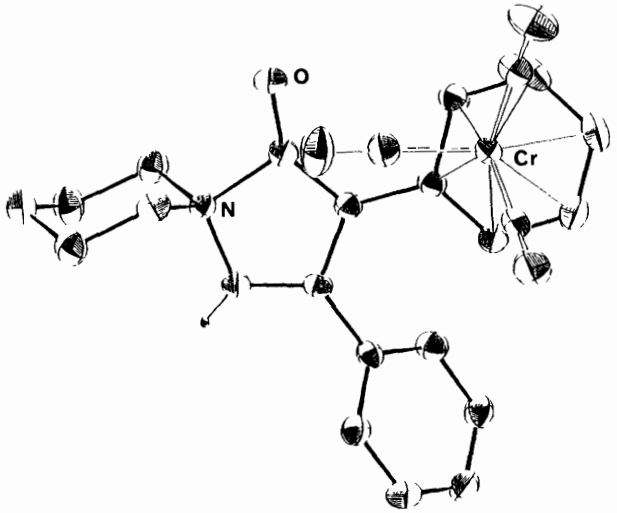
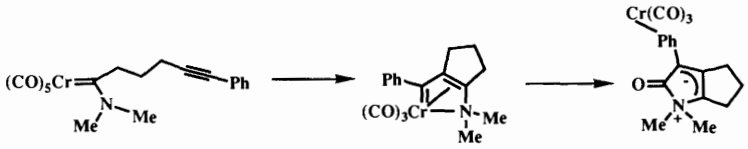


Figure 5

(74; R = CH_3,Ph) (75)

Scheme 31



(76) (77) (78)

Scheme 32

6 Rearrangement of the Ylide Intermediates: Nitrogen to Carbon Migrations of Alkyl Groups

Although stable in boiling benzene or cyclohexane, the isolated ylides underwent an easy rearrangement to the expected lactams upon heating for a few hours in refluxing toluene. Thus complex (70) gave the bridgehead lactam (89) in 70%

[52] A. Parlier, H. Rudler, and C. Alvarez, *J. Organomet. Chem.*, 1990, **379**, 271.

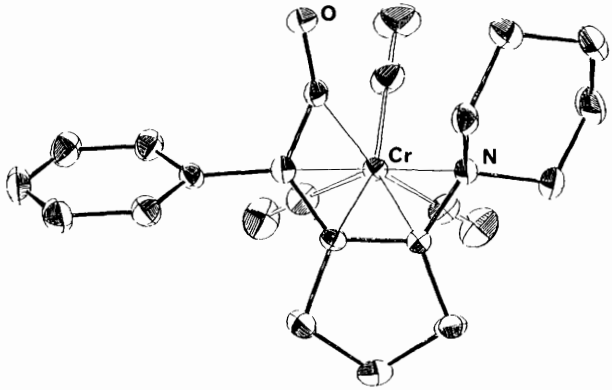


Figure 6

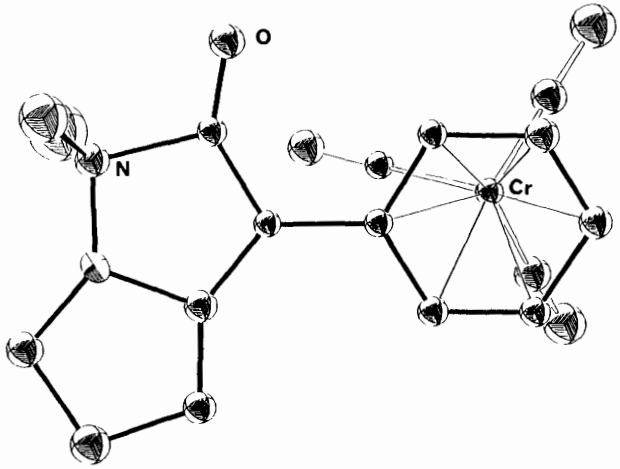


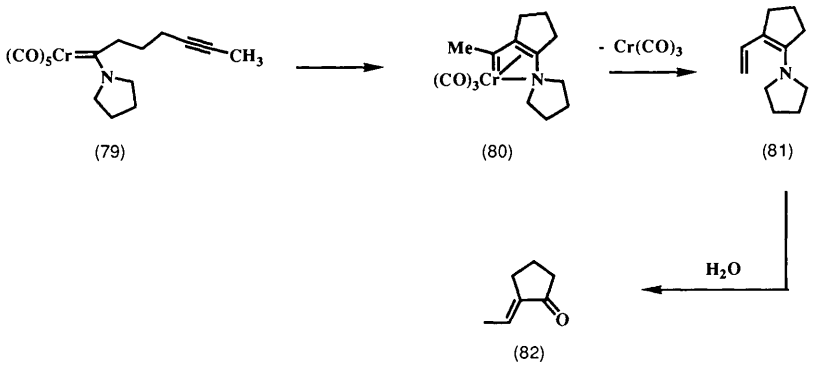
Figure 7

yield as the free organic product, whereas (75) under the same conditions led to the pyrrolinone (90). As in the previous cases where the ylides could not be isolated, nitrogen to carbon migrations occurred, providing strong evidence for the suggested mechanism (Schemes 36 and 37).[50]

7 The Case of a Phenyl-substituted Carbene Complex: Nitrogen to Oxygen Migration of a Vinyl Group

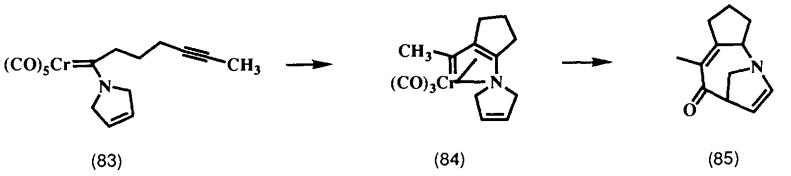
A few examples of aryl group migrations have been observed during the Stevens rearrangement of N-ylides. It was therefore of interest to examine the behaviour of *N*-phenyl aminocarbene complexes such as (91) in their reaction with alkynes. Surprisingly, we did not observe the same behaviour for the intermediate ylide.

Complex (91) reacted in boiling benzene with diphenylacetylene to give, as sole



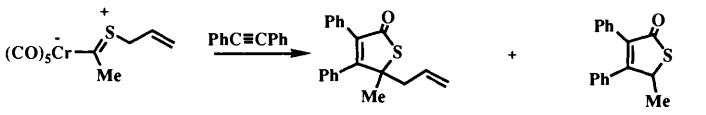
(79) (80) (81) (82)

Scheme 33



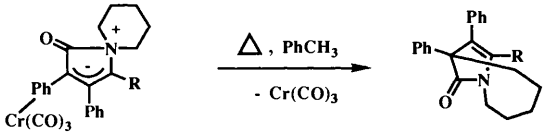
(83) (84) (85)

Scheme 34



(86) (87) 40% (88) 4%

Scheme 35

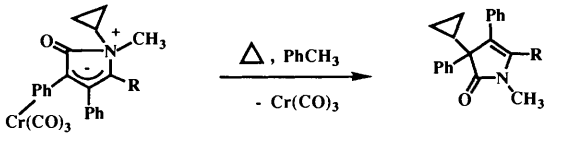


(70, R = H, CH_3) (89)

Scheme 36

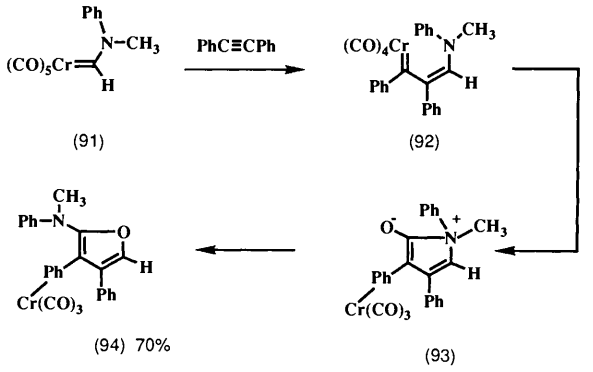
product, complex (94) (70%), which is indeed the result of the migration of the vinyl group from nitrogen to the oxygen atom of the carbonyl group of the intermediate ylide (93) (Scheme 38).[50]

8 Aminocarbene Complexes Derived from Primary Amines: Pyrrolinone Formation upon Alkyne/CO Insertions and Nitrogen to Carbon Migrations of Hydrogen in Molybdenum Carbene Complexes



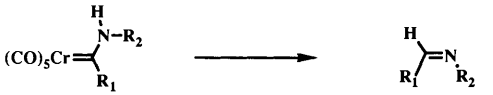
(75, R = CH_3, Ph) (90)

Scheme 37



(91) (92) (93) (94) 70%

Scheme 38



(95) (96)

Scheme 39

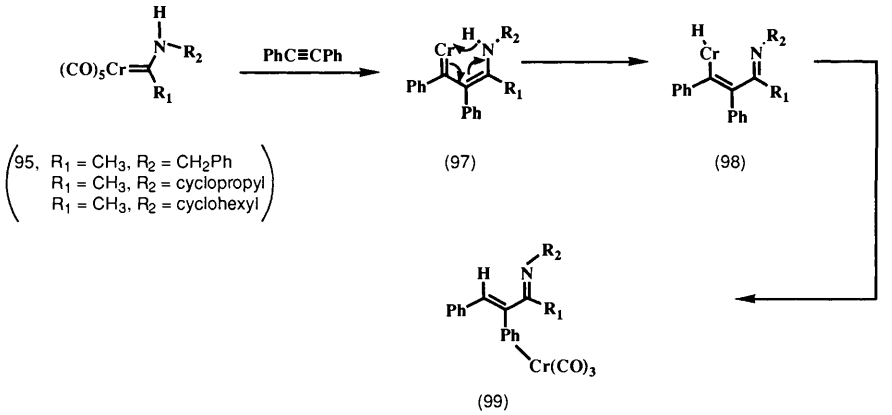
The thermolysis of aminocarbene complexes (95) derived from primary amines was investigated soon after their discovery. It was found that displacement of the aminocarbene ligand occurred in boiling pyridine, resulting in the formation of imines (96).[53] This reaction can be explained in terms of the insertion of a carbene into a N–H bond (Scheme 39).

We found that aminocarbene complexes of chromium of general structure (95) react with PhC≡CPh in boiling benzene to give the imines (99) as main products (70% yield).[54] Thus, from a formal point of view, alkyne insertion followed by the insertion of the newly formed carbene complex (97) into the N–H bond (or a 1,5 hydrogen migration followed by a reductive elimination (97) ⟶ (98) ⟶ (99) had taken place (Scheme 40). However, no CO insertion was observed.

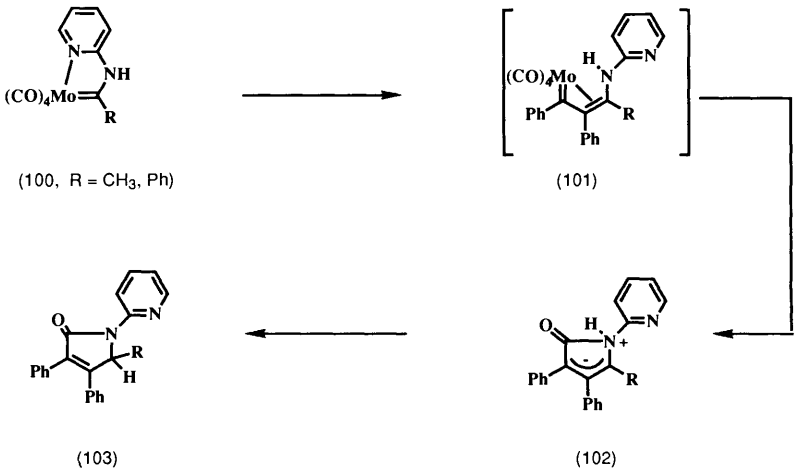
Such was not the case however for the molybdenum carbene complexes derived from aminopyridine (100; R = CH_3, Ph). In contrast to their chromium

[53] E O Fischer and M Leupold, *Chem Ber*, 1972, **105**, 599

[54] B Denise, P Dubest, A Parlier, M Rudler, H Rudler, J C Daran, J. Vaissermann, F Delgado, A R Arevalo, R A Toscano, and C Alvarez, *J Organomet Chem*, 1991, in press



Scheme 40

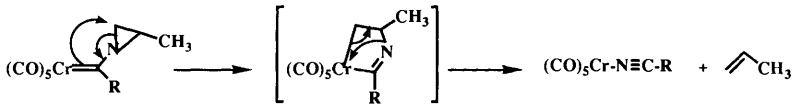


Scheme 41

analogues they behaved like aminocarbene complexes derived from secondary amines—upon alkyne/CO insertions, probably *via* (101) and (102), they gave pyrrolinones (103) in 40% yield. These pyrrolinones are the expected products of the interaction of a secondary amine with a conjugated ketene, as in (102) (Scheme 41)[54]

9 Special Case of Aziridino-substituted Carbene Complexes: Double Alkyne Insertion followed by CO Insertion: Formation of Indolizine Derivatives

Among aminocarbene complexes of chromium, aziridinocarbene complexes (104) revealed a special behaviour: in contrast to the examples so far examined, they



(104 R = CH_3 Ph *o* tolyl) (105) (106) (107)

Scheme 42

(108) (109)

Scheme 43

were not stable in boiling benzene or cyclohexane and rearranged *per se* to nitrile complexes (106) and olefines (107) (Scheme 42)[55] A mechanism for this transformation, the first step of which, (104) ⟶ (105), is reminiscent of the rearrangement of N-acylaziridines (108) into oxazolines (109), is given in Schemes 42 and 43

However, in the presence of alkynes, their transformation as in Scheme 42 did not take place Instead, a double insertion of the alkyne together with a single insertion of CO, and then ring-opening, led to oxatetrahydroindolizine complexes (111) whatever the substituents on the carbene carbon atoms, the dihydropyridine moiety was co-ordinated to a chromium tricarbonyl group [19 20]

It is obvious that in this last case neither ketene nor ylide intermediates were formed since no lactam function was present in the final products

A possible mechanism, which relies on the thermal rearrangement of complexes (104), is a direct ring-opening of (104) followed by a double alkyne insertion reaction to product (110) Electrocyclization followed by CO insertion might then lead to complexes (111) (Scheme 44) [3 19]

10 General Discussion

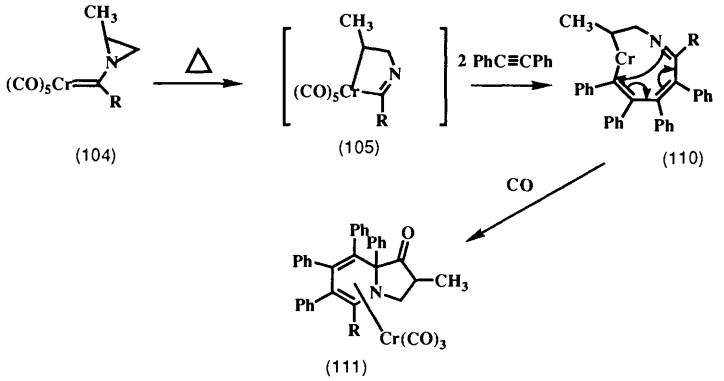
In the light of the results gathered up to now, a general scheme which provides a mechanism for the insertion of alkynes into aminocarbene complexes can be given

(i) The transformation of (79) into (82) confirms that the first step of the reaction is the insertion of the alkyne

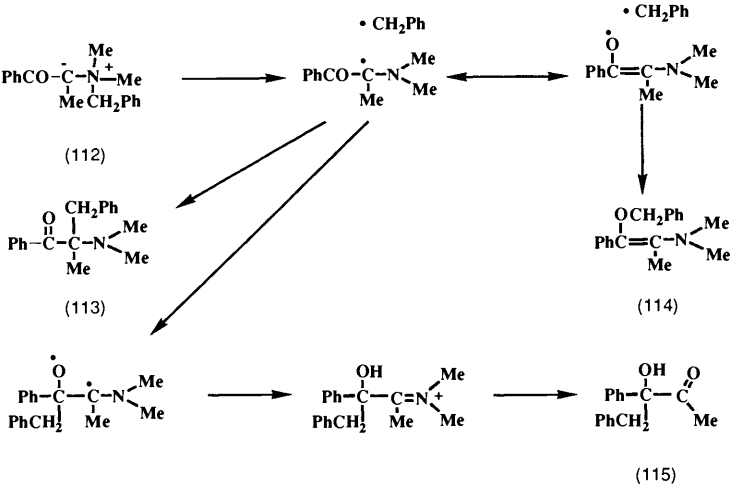
(ii) The formation of cyclopropanes when the allylic groups are *cis* with respect to the metal is not indicative of an aza-Claisen type rearrangement[35] for the formation of the reaction products

(iii) The isolation of ylide intermediates (70), (75), and (78) demonstrates that the second step is the CO insertion with formation of an enaminoketene which upon an intramolecular reaction gives the N-ylides

[55] B Denise A Massoud A Parlier H Rudler J C Daran J Vaissermann C Alvarez R Patino and R A Toscano *J Organomet Chem* 1990 **386** 51



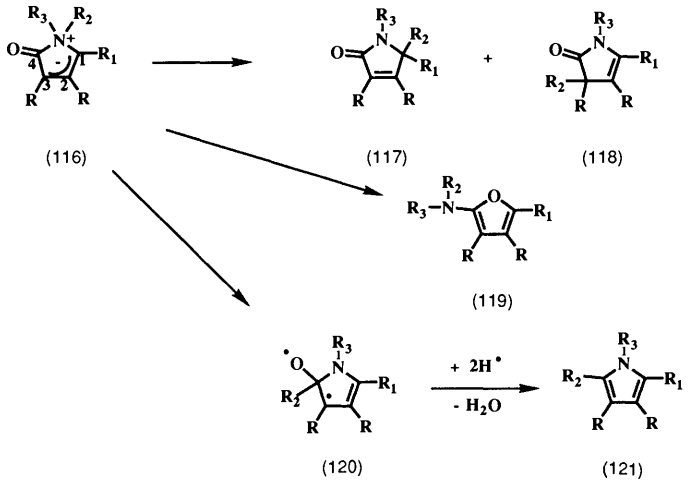
Scheme 44



Scheme 45

The rearrangement of these ylides can lead to a large variety of new heterocyclic compounds, depending on the site of transfer of the nitrogen substituents. As already mentioned, all the results observed so far parallel those for the Stevens rearrangement of chemically generated N-ylides. Along the same lines and especially revealing is the rearrangement of ylide (112) (Scheme 45) which leads[47] to a large variety of products resulting from the migration of the benzyl group to the adjacent carbon atom to give (113), or to the oxygen of the carbonyl group to give (114), or finally to the carbon of the carbonyl group to give (115).[47]

It is significant that most of these types of migrations have been observed



Scheme 46

during the rearrangement of N-ylides (116) obtained from aminocarbene complexes (Scheme 46):

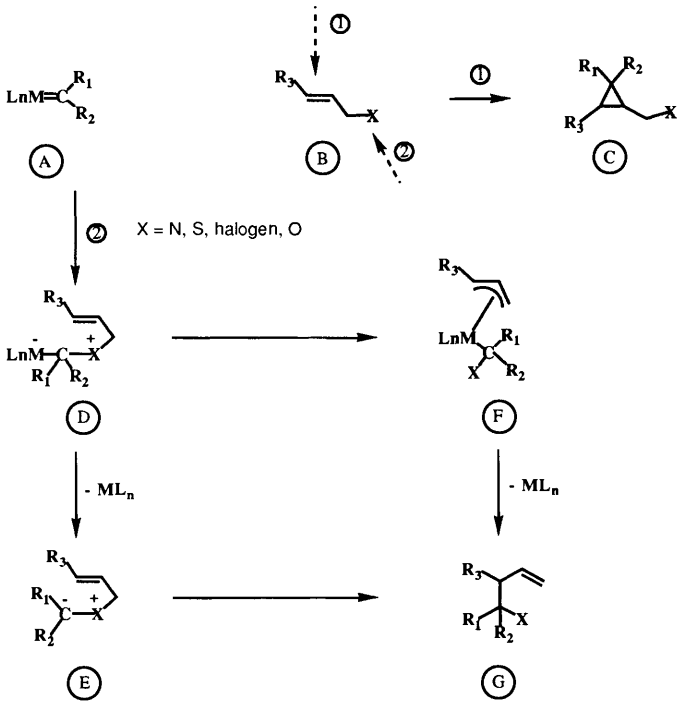
(i) Migration to C-1 (or the vinylogous C-3) giving (117) or (118).

(ii) Migration to oxygen in the case of *N*-phenyl substituted aminocarbene complexes giving (119).

(iii) And finally migration to C-4, a reaction leading to the pyrroles (121) in the case of the pyrrolidine-substituted complexes; this last reaction is the most complicated one since, after the migration of the alkyl chain leading to (120), hydride abstractions and dehydration must take place, with or without the help of the metal.

It is now possible to sketch a parallel between the behaviour of carbene complexes generated from Fischer carbenes and alkynes, and carbene complexes generated from diazo-compounds and rhodium or copper derivatives.[41] Common to both systems are their reactions with alkenes to give cyclopropanes, with aromatics to give annulated products, and with activated and non-activated hydrogens to give insertion products. Nevertheless, differences between the two systems can easily be detected. First, whereas the rhodium system works catalytically, the chromium system needs stoicheiometric amounts of carbene complexes. However, in most cases this drawback is minimized since CO insertions take place without the need for external CO. The second and most important difference is their interaction with heteroatoms (N,S) which is highly dependent on the nature of the ligands on the metal. In the case of rhodium, heteroatoms interact directly with the carbenes, whereas in the case of chromium this interaction promotes the insertion of CO, and thus the formation of ketenes[49,56–59] and only then of ylides.

Simplified general mechanisms for these two systems appear in Schemes 47

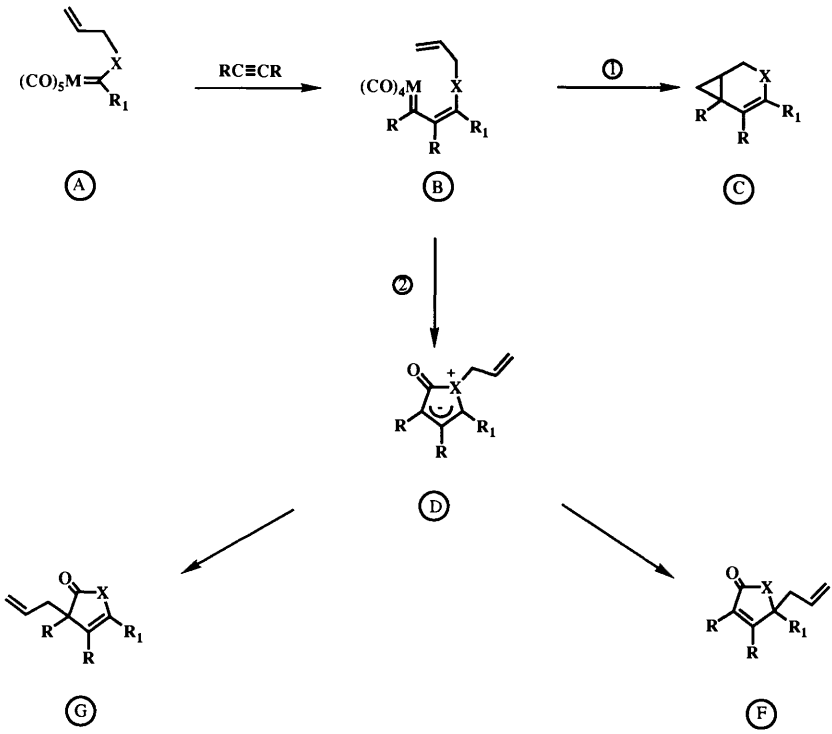


Scheme 47

and 48. In the first case, decomposition of diazo-compounds in the presence of unsaturated substrates is illustrated in the scheme: the rhodium carbene complex A reacts with the substrate, containing a double bond and a heteroatom X, to give a mixture of products. Reaction according to 1 gives the cyclopropane C and reaction according to 2 gives the ylide D. D might in turn loose the metal MLn to give the organic ylide E. Finally, rearrangement according to the allowed (3,2) concerted migration gives G.

In the case of chromium, a requisite for the observation of the interesting and unprecedented transformations is the insertion of an alkyne into A, a stable amino-carbene complex which can easily be modified structurally. This reaction leads to a new very reactive complex B. The structure of A (*E* or *Z* isomer) directly affects the direction of the transformation of B: *Z* gives the cyclopropane C and *E* leads to the ylide D which then undergoes the observed rearrangements to F and G.

[56] A. Herrmann and J. Plank, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 525.
[57] H. Rudler, J. Levisalles, and D. Villemin, *J. Organomet. Chem.*, 1978, **146**, 259.
[58] H. Fischer, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 874.
[59] B. Denise, D. Navarre, H. Rudler, and J. C. Daran, *J. Organomet. Chem.*, 1989, **375**, 273.



Scheme 48

Surprisingly, it is only very recently[60] that Scheme 48 has been applied to the rhodium carbene complexes for the generation of very reactive carbene complexes. It has indeed been shown that the carbene complexes obtained from diazo-compounds react with alkynes in the same way as chromium carbene complexes do to give vinylidene carbene complexes such as B which can undergo various transformations, *inter alia* intramolecular cyclopropanations.

11 Conclusion

As a general conclusion, all examples outlined in the present account reveal aspects of Fischer carbene complexes which were unsuspected up to now and which broaden even more the scope of their applications in organic chemistry. It has become evident that amino- and thiocarbene complexes of chromium represent a class of compounds, the reactivity of which is very original. Most aspects of their new chemistry, such as the ylide formation and transformation, have been unravelled. Some others, for example the exact mechanism of the alkyl migration reaction (concerted or non-concerted migrations, involvement or not

of the metal in this last step *etc.*) are still under investigation. It is clear that further work in this field will lead to new synthetic spin-offs despite the fact that this type of carbene complex has now been known for a quarter of a century.

[60] A. Padwa, U. Chiacchio, Y. Garreau, J. M. Kassir, K. E. Krumpe, and A. M. Schoffstall, *J. Org. Chem.*, 1990, **55**, 414.