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SYNTHESIS OF INDENES FROM ALKYNES AND PHENYL AMINO CHROMIUM CARBENE COMPLEXES

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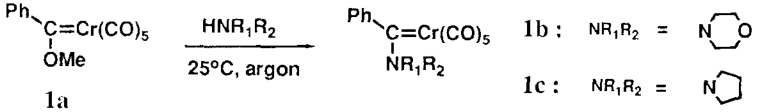
ABSTRACT: Reactions of phenyl morpholino or pyrrolidino chromium carbene complexes with alkynes in DMF at 120-125°C resulted in exclusive formation of the indene derivatives.

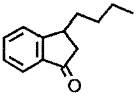
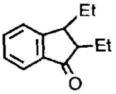
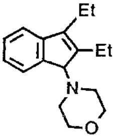
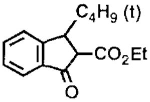
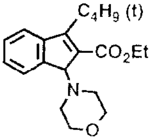
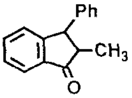
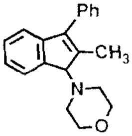
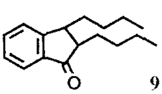
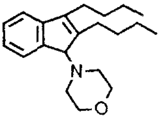
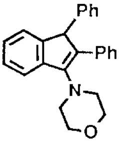
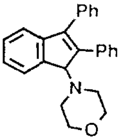
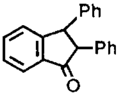
The reaction of pentacarbonyl[phenyl(methoxy)carbene]chromium (**1a**) with diphenylacetylene in heptane has been previously reported to provide the benzannulated products (naphthols) as major components along with indenes, furans, and cyclobutenone.[1] This was the first indication of the complexity of the alkyne-carbene reaction with regard to structural variations in the products and sensitivity to the reaction conditions. Although the naphthol is the normal product from the carbene-alkyne cycloaddition reaction[2], indene [2d,3], furan[4] and cyclobutenone [2d,4,5] have been observed on rare occasions or as minor products. We report here that the reaction of pentacarbonyl-[phenyl(morpholino or pyrrolidino)carbene]chromium with an alkyne in DMF at 125°C results in exclusive formation of the indene derivatives. This is the first example of the amine substituted chromium carbene complex participating the carbene-alkyne cycloaddition process.



Scheme 1

The phenyl morpholino carbene complex (**1b**) and the phenyl pyrrolidine carbene complex (**1c**) were prepared from **1a** with amines according to the procedure of E.O. Fischer (Scheme 1).[6] A DMF solution of **1b** (or **1c**) and an alkyne (1.5 - 2.0 mol eq) was heated at 120-125°C (bath temperature) for 5 hrs under argon, at which time TLC analysis indicated that the complex was consumed. The bath temperature was reduced to 90-95°C, and the reaction mixture was heated for an additional 15 hr for complete reaction. The mixture was cooled and diluted with ether. The ether layer was washed with saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated by rotary evaporation. The products were isolated by silica gel flash column chromatography. Table 1 presents the results from the reactions of **1b** or **1c** with alkynes.[7] The complex **1b** reacted with 1-hexyne to produce the

Table-I : Reactions of 1b and 1c with alkynes in DMF at 125 °C

Entry	Alkyne[*a]	Carbene complex	Product (%)[*b]		
1	$H-C\equiv C-C_4H_9$ (n)	1b	 2 (95)		
2	$H-C\equiv C-C_4H_9$ (n)	1c	2 (49)		
3	$Et-C\equiv C-Et$	1c	 3 (52)		
4	$Et-C\equiv C-Et$	1b	 4 (96)		
5	(t) $C_4H_9-C\equiv C-CO_2Et$	1b	 5 (31)	+	 6 (58)
6	$Ph-C\equiv C-CH_3$	1b	 7 (41)	+	 8 (52)
7	(n) $C_4H_9-C\equiv C-C_4H_9$ (n)	1b	 9 (28)	+	 10 (67)
8	$Ph-C\equiv C-Ph$	1b	 11a (55)	+	 11b (34)
9	$Ph-C\equiv C-Ph$	1b	 12 (52)	+	11b (34) [*c]

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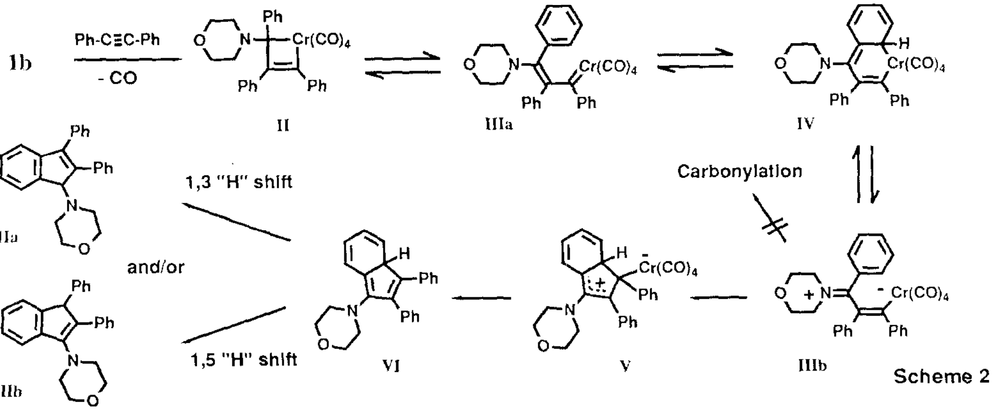
*a : 1.5 - 2.0 mol eq of alkyne was used. *b : Isolated yield. *c : Followed by acid treatment.

indanone (**2**) as the only product in 95% yield (entry 1). However, under the same conditions, **1c** gave **2** in 49% yield (entry 2). In contrast to the 1-hexyne case, the reaction of **1b** with 3-hexyne provided exclusively the allylic amine (**4**) in 96% yield (entry 4). Alkynes such as ethyl-4,4-dimethylpentynoate (entry 5), phenylpropyne (entry 6) and 5-decyne (entry 7) resulted in formation of indanones (**5, 7, 9**) and allylic amines (**6, 8, 10**) in an approximate ratio of 1:1 - 1:2. The indanone presumably arises from hydrolysis of the corresponding enamine during the isolation process. Compared with **1b**, **1c** produced indanones in lower yields (entry 2, 3)[8].

The reaction of **1b** with diphenylacetylene afforded the enamine (**11a**) and the allylic amine (**11b**) in 55% and 35% yield, respectively. The structural difference between **11a** and **11b** was determined by the rate of acid hydrolysis (1 N HCl/MeOH, 25 °C, 24 hrs), where **11a** was converted to the corresponding indanone (**12**) while **11b** remained unchanged under the same conditions. This was also supported by conducting the same reaction, followed by acid treatment, to give a 52% yield of **12** and a 34% yield of **11b** (entry 9). It was noticed that only in this case where both conjugatively stabilizing substituents and an amine of lesser nucleophilicity are present can the enamine be isolated. DMF as a solvent and the high reaction temperature seems to be essential for efficient indene formation.[9] For example, heating a THF solution of **1b** with diphenylacetylene at 65°C for 7 days provided a 33% yield of a mixture of **11a** and **11b** (approximately 1 : 1 ratio) with a 27% yield of recovered **1b**.



Scheme 2

A plausible pathway for formation of indene derivatives is outlined in Scheme 2 for **1b** with diphenylacetylene. According to the previously proposed mechanism,[4,10] the ring-opening of metallocyclobutenone (II) would lead to the coordinatively unsaturated intermediate (IIIa), which may form either metallocyclohexadiene (IV) or the tautomer (IIIb) by enamine resonance. Carbon monoxide insertion could be intercepted because of negatively charged metal anion of IIIb. Instead, a Nazarov-type cyclization from IIIb could be mediated by tetracarbonyl chromium probably accelerated by the high reaction temperature, forming the 5-membered ring (V).[11] Disassociation of tertracarbonyl chromium would be assisted by a polar solvent like DMF, to generate the intermediate (VI). Then, a 1,5- and/or a 1,3-proton shift from VI produces the allylic amine (VIIa) and/or the enamine (VIIb). The ratio of VIIa and VIIb appears to depend on the conjugation and a 1,3-steric interaction between the amine and the substituent at β-position. In the 3-hexyne reaction, the allylic amine **4** could be favored due to avoidance of a 1,3 steric strain between a morpholine ring and ethyl group in the corresponding enamine form.[12] However, in the 1-hexyne reaction, because of a lesser steric strain between a morpholine ring and a hydrogen at the β-position, the enamine form would be favored due to enamine resonance.

Further experiments directed toward an explanation of these observations are currently being pursued, and applications of this reaction to the synthesis of complex molecules will be reported in due course.

References

1. K.H. Dötz, *J. Organomet. Chem.*, **140** 177 (1977). From this reaction, the indene (**13**) and its chromium tricarbonyl complex were obtained in a 26% and 5% yield, respectively. The reaction of **1a** with diphenylacetylene in DMF at 85-90°C provided **13**, as the only product in an 83% yield.

13 (83 %)

2. For recent references on chemistry of carbene complexes with alkynes: a) K.H. Dötz, H. Fischer, P. Hoffmann, F.P. Kreissl, V. Schubert, K. Weiss, "Transition Metal Carbene Complexes," Verlag Chemie, Deerfield Beach, FL 1984. b) K.H. Dötz, M. Popall, *Tetrahedron*, **41** 5797 (1985). c) M.F. Semmelhack, J. Bozell, L. Keller, T. Sato, E.J. Spiess, W.D. Wulff, A. Zask, *Tetrahedron*, **41** 5803 (1985). d) W.D. Wulff, P.C. Tang, K.S. Chan, J.S. McCallum, D.C. Yang, S.R. Gilbertson, *Tetrahedron*, **41** 5813 (1985).
3. K.H. Dötz, R. Dietz, D. Kappenstein, D. Neugebauer, V. Schubert, *Chem. Ber.* **112** 3682 (1979).
4. W.D. Wulff, S.R. Gilbertson, J.P. Springer, *J. Am. Chem. Soc.*, **108** 520 (1986) and references herein.
5. a) K.H. Dötz, R. Dietz, *J. Organomet. Chem.*, **157** C55 (1978). b) A. Yamashita, T.A. Scahill, A. Toy, *Tet. Lett.*, 2969 (1985).
6. The complex **1b** was obtained as yellow crystals in 76% yield from the reaction of **1a** with an excess of morpholine. Similarly, **1c** was obtaned as yellow crystals in 80% yield from **1a** and pyrrolidine. a) U. Klabunde, E.O. Fisher, *J. Am. Chem. Soc.*, **89** 7141 (1967). b) K. Weib, E.O. Fisher, *Chem. Ber.*, **106** 1277 (1973). c.) B. Heckl, H. Werner, E.O. Fisher, *Angew. Chem., Int. Ed.* 7 817 (1968).
7. All new compounds (**2**, **3**, **4**, **5**, **6**, **7**, **8**, **9**, **10**, **11a**, **11b**, and **12**) have been characterized by satisfactory combustion and spectral (high resolution mass, IR, and ^{1}H-NMR) analysis. Compounds **3**, **5**, **7**, **9**, **12** were homogeneous by chromatographic and ^{1}H-NMR spectra analysis, but configuration of these products has not been assigned. Regiochemistry of two functional groups in **2**, **5**, **6**, **7**, and **8** was determined on basis of the earlier observations. A. Yamashita, A. Toy, *Tet. Lett.* **27**, 3471 (1986).
8. This presumed that, because of the steric strain in the intermediate **IIIb** derived from a 5-membered pyrrolidine ring, cyclization to V became less favored.
9. Indene formation using the following alkynes (ethyl propiolate, bis-trimethylsilylacetylene, 3-dimethylamino-propyne, dimethyl acetylenedicarboxylate, ethyl-3-phenylpropynoate) was unsuccessful under conditions described above.
10. a) K.H. Dötz, B. Fugen-Köster, *Chem. Ber.*, **113** 1449 (1980). b) H. Fischer, J. Mulheimer, R. Markl, K.H. Dötz, *Chem. Ber.*, **115** 1355 (1982).
11. a) I.N. Nazarov, I.I. Zaretskoya, *J. Gen. Chem. USSR* (Engl. Trans.), **27** 693 (1957). b) Recent work of Nazarov type reaction, T.K. Jones, S.E. Denmark, *Helv. Chim.*, **66** 2397 (1983), S.E. Denmark, T.K. Jones, *J. Am. Chem. Soc.*, **104** 2643 (1982) and references cited herein.
12. This explanation can't be applied to the 5-decyne reaction (entry 7), unless one presumes that the equilibrium **VIIa** ⇌ **VIIb** could change the product ratio. Further studies in this area are currently being investigated.

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