Pergamon

Tetrahedron Letters, Vol. 35, No. 21, pp. 3505-3508, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

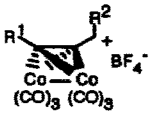
0040-4039(94)E0601-S

Transition Metal Mediated Three Component Coupling Reactions with Enamines[1]

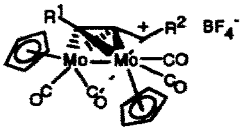
Klaus-Dieter Roth, Institut für Organische Chemie,
Universität Erlangen, Henkestr. 42, 91054 Erlangen

Abstract: Reactions of molybdenum stabilized propargyl cations **2** with enamines are described, constituting a molybdenum mediated analogue of the Nicholas reaction and extending the scope of propargylations of enamines by means of transition metal complexed carbocations.

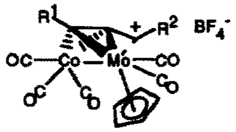
Dinuclear transition metal alkyne complexes have received an increasing deal of interest from synthetic organic chemists during the past two decades and thus have become versatile and powerful reagents for organic syntheses. Especially interesting in this context are transition metal stabilized propargyl cations. The $Co_2(CO)_6$-alkyne complexes **1** are the most thoroughly investigated class of compounds in this field. Reactions with nucleophiles, commonly termed *Nicholas reactions*, have been extensively studied. For the most part carbon nucleophiles were used,[2,3] but Nicholas reactions with O-,N- and S-nucleophiles are also known.[4-6] Recently research also has focused on the $[CpMo(CO)_2]_2$-analogues **2** and the corresponding mixed metal compounds, $CpMo(CO)_2Co(CO)_3$-alkyne complexes **3**. A few reactions of molybdenum stabilized propargyl cations **2** with nucleophiles were reported,[7,8] but no use has been made so far of these compounds for organic syntheses.



1

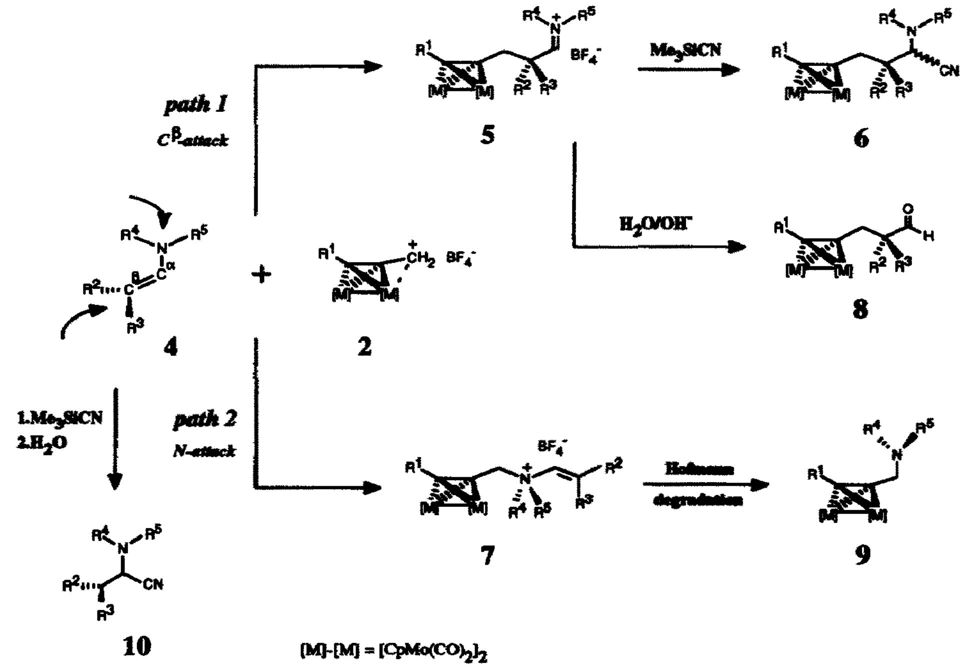


2



3

Recently we described the first successful Nicholas reactions with enamines as nucleophiles.[1] In the course of these investigations we found that only N,N-dibenzyl- or N,N-diallylenamines can be used under our experimental conditions, which interferes with the generality of this reaction protocol. Therefore it was decided to examine the reactions of cationic $[CpMo(CO)_2]_2$-allenyl complexes with enamines. From our experiences with the analogous $Co_2(CO)_6$-compounds we expected the reaction to follow exclusively *path 1* in the general reaction scheme (Scheme 1). Attack of the metal stabilized propargyl cation **2** at the β-carbon atom of the enamine **4** should lead to a complexed 4-alkynyliminium ion **5**. Treatment of this electrophilic intermediate with another nucleophile (Me_3SiCN) should then give the neutral complex **6** as the result of a three component coupling reaction (3-CC reaction) between the coordinated carbocation, the enamine and the nucleophile. Since molybdenum cations of type **2** are soluble in acetone the first reactions with enamines were run in this solvent. The analysis of the product composition obtained under this conditions revealed a more complex pattern of reactivity of the cationic species. In most runs in acetone we isolated a product mixture with always poor yields of the desired three component coupling compounds (see Table 1), together with a mixture of molybdenum coordinated 4-alkynals and propargyl amine complexes. The formation of the aldehydic compounds can be explained by hydrolytic cleavage of unchanged iminium ion, but the propargyl amine compounds can only be formed via attack of the metal complexed cation at the *enamine nitrogen*. This behaviour of the metal stabilized carbocation was never encountered in the related Nicholas reactions. Since the formation of such amine complexes could be observed in all the solvents we used (see Table 1), the reaction scheme had to be extended (*path 2*) to account for the experimental results, leading us to the complete general reaction scheme shown below.



Scheme 1

Attack of the molybdenum complexed carbocation at the β-carbon of the enamine yields the desired alkynyliminium ion **5**, whereas addition of the electrophile to the enamine nitrogen should give a coordinated alkinylammonium ion **7**. A Hofmann degradation of the latter intermediate, presumably during aqueous workup, would then lead to the observed propargyl amine compounds **9**.[9] The alkynyliminiumion as intermediate can undergo nucleophilic addition of a cyanide ion (from TMSCN) to yield finally molybdenum complexed α-aminonitriles **6** whereas the isolated aldehydic complexes **8** are byproducts, arising from an incomplete reaction of the intermediate with TMSCN and subsequent hydrolysis of remaining iminium salt.

As the coupling reactions did not proceed in the desired manner in acetone, we decided to change the solvent to acetonitrile, but the results, revealing an almost complete absence of regioselectivity, were equally disappointing (see Table 1, entries *4,5,6*). The main feature of the reactions run in acetonitrile, when compared to acetone, is an increased yield of a completely unexpected side product **10**, formally resulting from addition of hydrogen cyanide to the starting enamine. At present we have no reasonable explanation for the formation of such metal free α-aminonitriles, but this problem is currently under investigation.[10]

The next set of reactions was conducted in DME, which was successfully used as solvent in Nicholas reactions of enamines. Under these heterogeneous conditions the molybdenum coordinated electrophile displayed a significantly

Table 1: Reactions of cationic molybdenum complexes **2** with enamines **4**[a]

entry	**2**	**4**	solvent	yield [%] **6**	**8**	**9**	**10**
1	R^1 = H	R^2,R^3 = CH_3		a	a	a	
		R^4,R^5 = $CH_2C_6H_5$	acetone	-	25	62	-
			DME	59	-	16	-
2	R^1 = H	R^2,R^3 = CH_3			a	b	
		R^4,R^5 = $CH_2CH{=}CH_2$	acetone	-	30	61	-
3	R^1 = H	R^2,R^3 = CH_3		b	a	c	
		R^4,R^5 = $(CH_2CH_2)_2O$	acetone	11	32	48	-
4	R^1 = CH_3	R^2 = CH_3, R^3 = C_6H_5		c	b	a	a
		R^4,R^5 = $CH_2C_6H_5$	acetone	33	5	20	20
			CH_3CN	29	30	28	10
			DME	33	-	8	28
5	R^1 = CH_3	R^2 = H, R^3 = C_6H_5		d	c	a	
		R^4,R^5 = $CH_2C_6H_5$	acetone	30	23	10	-
			CH_3CN	33	36	13	-
			DME	73	-	-	-
6	R^1 = CH_3	R^2,R^3 = CH_3			a	a	b
		R^4,R^5 = $CH_2C_6H_5$	CH_3CN	-	41	33	32
7	R^1 = H	R^2 = H, R^3 = C_6H_5		e		a	
		R^4,R^5 = $CH_2C_6H_5$	DME	67	-	4	-
8	R^1 = CH_3	R^2 = H, R^3 = C_6H_5		f	c		
		R^4,R^5 = $(CH_2CH_2)_2O$	acetone	22	56	-	-
			DME	75	-	-	-

[a] Yields are of isolated products after chromatographic purification,[11] all new compounds were characterized by ^1H, ^{13}C NMR and mass spectroscopy and gave satisfactory elemental analyses.[12]

increased regioselectivity (Table 1, entries *1,4,5,7,8*). In most runs the desired three component coupling products could be isolated in reasonable to good yields together with only minor amounts or no amine complex at all. The only exception is the reaction with the N,N-dibenzylenamine derived from hydratopaaldehyde (entry *4*), but this compound displayed a particularly unselective behaviour in all reactions examined. The reaction conditions of the entries in Table 1 are not optimized, therefore it should be possible to increase both regioselectivity and yield to obtain exclusively the desired molybdenum coordinated α-aminonitriles.

The main feature of the described molybdenum initiated tandem electrophile/nucleophile additions to enamines is, as the results indicate (entries *3* and *8* in Table 1), the possibility to use also enamines derived from amine components other than dibenzyl- or diallylamine in these 3-CC reactions, which is the major restriction of the related Nicholas reaction. Provided that optimal reaction conditions can be elaborated for all kinds of enamines, this molybdenum mediated double functionalization of enamines can successfully complement the Nicholas reaction. Further investigations concerning the stereochemistry of the reaction products, methods of decomplexation to the metal free compounds and the yet not well understood influence of the solvent on the product distribution are currently underway.

References and Notes

1. Part 1: Roth, K.-D. *Synlett* **1992**, 435.
2. a) Nicholas, K.M. *Acc. Chem. Res.* **1987**, *20*, 207 and references cited therein b) Schreiber, S.L.; Klimas, M.T.; Sammakia, T. *J. Am. Chem. Soc.* **1987**, *109*, 5749 c) Stuart, J.G.; Nicholas, K.M. *Synthesis* **1989**, 454 d) Jacobi, P.; Zheng, W. *Tetrahedron Lett.* **1993**, *34*, 2581.
3. a) Roth, K.-D. *Synlett* **1993**, 529 b) Nakagawa, M.; Ma, J.; Hino, T. *Heterocycles* **1990**, *30*, 451.
4. Smit, A.; Schegolev, A.A.; Gybin, S.; Mikaelian, G.S. *Synthesis* **1984**, 887.
5. a) Roth, K.-D.; Müller, U. *Tetrahedron Lett.* **1993**, *34*, 2919 b) Jeong, N.; Yoo, S.; Lee, S.J.; Lee, S.H.; Chung, Y.K. *Tetrahedron Lett.* **1991**, *32*, 2137.
6. a) El-Amouri, H.; Gruselle, M.; Jaouen, G.; Daran, J.; Vaissermann, J. *Inorg. Chem.* **1990**, *29*, 3238. b) Bennett, S.C.; Gelling, A.; Went, M.J. *J. Organomet. Chem.* **1992**, *439*, 189.
7. Meyer, A.; McCabe, D.J.; Curtis, M.D. *Organometallics* **1987**, *6*, 1491.
8. a) Gruselle, M.; Philomin, V.; Chaminant, F.; Jaouen, G.; Nicholas, K.M. *J. Organomet. Chem.* **1990**, *399*, 317 b) Le Berre-Cosquer, N.; Kergoat, R. *Organometallics* **1992**, *11*, 721.
9. The assumed way of formation of the amine complexes *via* Hofmann degradation is supported by the result of the reaction of **2a** with NEt_3 and Me_3SiCN, which yields the corresponding propargyldiethylamine complex as product of the proposed elimination reaction.
10. In all reactions of the 3-trimethylsilylsubstituted molybdenum cation (**2**, $R^1 = SiMe_3$) with enamines and TMSCN we observed the *exclusive* formation of metal free α-aminonitriles of general formula **10** in good yields.
11. To a slurry of 2 mmol molybdenum complex **2** in 60 mL of dimethoxyethane (DME) is added a solution of 2 mmol enamine **4** in 30 mL of DME. After 2h of stirring at ambient temperature 2.6 mmol Me_3SiCN are added and stirring is continued for 12 - 16 h. The reaction mixture is poured into 70 mL of a satd. solution of $NaHCO_3$, the organic layer is separated and the aqueous layer extracted with 100 mL of ether. The combined organic phases are dried over $MgSO_4$ and concentrated under reduced pressure. The residue is purified by column chromatography on silica gel with hexane/ether as eluent.
12. NMR data for representative compounds: **9c** ^1H NMR ($CDCl_3$, TMS): δ 2.49 (t, J=4.59 Hz, 2x2H), 3.56 (s, 2H), 3.63 (t, J=4.59 Hz, 2x2H), 5.29 (s, 10H), 6.04 (s, 1H); ^{13}C NMR ($CDCl_3$, TMS): δ 53.3, 62.8, 67.1, 85.1, 91.3, 232.8 . **6c** ^1H NMR ($CDCl_3$, TMS): δ 2.17 (br s, 3H), 3.14 (m, 2H), 3.30 (d, J=14.04 Hz, 2H), 3.33 (d, J=11.8 Hz, 1H), 3.60 (m, 1H), 3.88 (d, J=14.04 Hz, 2H), 4.98 (s, 5H), 5.16 (s, 5H), 6.91-7.38 (m, 15H); ^{13}C NMR ($CDCl_3$, TMS): δ 23.9, 40.3, 47.5, 55.1, 59.5, 61.8, 92.1, 92.3, 102.9, 116.7, 127.4, 127.7, 128.3, 128.6, 129.1, 137.1, 139.2, 233.7, 234.0 .

(*Received in Germany* 2 *February* 1994; *accepted* 22 *March* 1994)