Ligand and solvent effects on cobalt(I)-catalysed reactions: Alkyne dimerisation versus [2+2+2]-cyclotrimerisation versus Diels–Alder reaction versus [4+2+2]-cycloaddition

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Abstract

The cobalt catalysed conversion of phenyl acetylene led to linear enyne dimerisation products when $CoBr_2(dppe)$ was activated with magnesium in the absence of a Lewis acid. In contrast, in the presence of a Lewis acid the cyclotrimerisation process is favoured. Among several ligand systems and solvents tested the best results were obtained using a catalyst system consisting of a diimine cobalt bromide complex, zinc and zinc iodide in acetonitrile. With 2–5 mol% of the cobalt catalyst at ambient temperatures 1,2,4-triphenylbenzene could be obtained in 99% yield and in excellent regioselectivity (95:5) in 10 min reaction time. Competition experiments of phenylacetylene and isoprene were performed. A preference for the cyclotrimerisation reaction was found for the diimine cobalt complex in acetonitrile, while the Diels–Alder reaction is favoured with the cobalt(dppe) complex in dichloromethane. Also a regioselectively substituted cyclooctatriene product was formed in a [4+2+2]-cycloaddition process and isolated which allows assumptions on the reaction mechanism.
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1. Introduction

Transition metal complexes with vacant coordination sites are able to form complexes with unsaturated organic molecules such as alkenes or alkynes. These organic molecules can be activated within the ligand sphere of the transition metal to undergo carbon–carbon bond formation processes. When the liberation of the organic product regenerates the active species a catalytic process becomes possible. Accordingly, organic transformations with carbon carbon bond formations can be realised which would not be possible under regular thermal conditions in the absence of the transition metal. Among

such transformations, cycloaddition processes, such as the transition metal catalysed Diels–Alder reaction or the [2+2+2]-cyclotrimerisation of alkynes, are already well documented [1]. Over the last couple of years, we have investigated cobalt(I)-catalysed Diels–Alder reactions between non-activated terminal as well as internal alkynes and acyclic 1,3-dienes. We found that a catalyst system consisting of $Co(dppe)Br_2/ZnI_2/Bu_4NBH_4$ or zinc as reducing agent proved to be highly effective in the generation of dihydroaromatic compounds under mild reaction conditions in good to excellent yields [2]. In the earliest report of such transformations, we described the [2+2+2]-cyclotrimerisation of an acetylene carboxylic ester to the corresponding trisubstituted benzene derivative, which was an undesired side product at that point [3]. Besides the acetylene carboxylic ester, the cobalt catalyst system exhibits only a very low reactivity

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for the cyclotrimerisation of other terminal alkynes. Therefore, we started an investigation to determine the factors that would enhance the activity of the very inexpensive and easy to handle cobalt catalyst system towards carbon carbon bond formations.
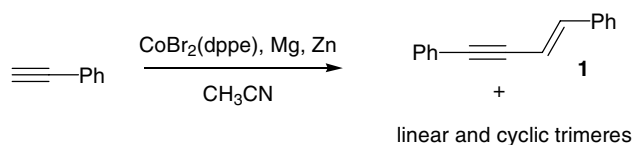
2. Results and discussion

For the cobalt-catalysed Diels–Alder reaction of alkynes with acyclic 1,3-dienes we proposed a cationic cobalt(I)-species as the active catalyst. This species is generated upon reduction and halide abstraction processes starting from $CoBr_2(dppe)$ as a catalyst precursor (Scheme 1) [4].

We envisaged that with a stronger reducing agent such as magnesium a second reduction process could take place to obtain a neutral cobalt(0)(dppe)-species with different reactivity in the reaction with unsaturated starting materials such as phenylacetylene.

2.1. Dimerisation process

The first experiments with the $CoBr_2(dppe)$ catalyst proved to be unsuccessful in dichloromethane as solvent, while in an acetonitrile/dichloromethane solvent mixture small amounts of the dimerisation product could be isolated [5]. Better results were obtained when acetonitrile alone was used as solvent. In these reactions a dimer accompanied by a mixture of linear and cyclic trimers (confirmed by GC–MS) of phenylacetylene was isolated. The dimer **1** could be easily separated from the trimers by column chromatography and was identi-

fied as (E)-1,4-diphenyl-but-1-en-3-yne (**1**) (Scheme 2) [6]. A thermal pre-treatment of the catalyst components in the absence of phenylacetylene was found to have a major effect on the reaction time. Prior to substrate addition the reaction time could be reduced from 20 h to only 10 min for complete conversion of the substrate.

An only slight effect on the product ratio was found when the ratio of the reducing agents magnesium and zinc was altered. Nevertheless, in the absence of zinc, using magnesium as the sole reducing agent (E)-1,4-diphenyl-but-1-en-3-yne (**1**) was obtained as major product after a few minutes reaction time when the catalyst was briefly heated to reflux prior to the addition of the starting material (compare Table 1, entries 2 and 7). A combination of magnesium and zinc as reducing agents yields trimers as main products. However, the reaction proceeds without magnesium and with zinc as reducing agent very slowly (Table 1, entry 8).

The formation of linear and cyclic trimers could not be reduced significantly, so that only moderate yields (47%) of the dimerisation product **1** could be obtained as the best result (Table 1, entry 7). Further investigations towards a synthetically useful chemo- and regiochemically pure dimerisation process were not conducted.
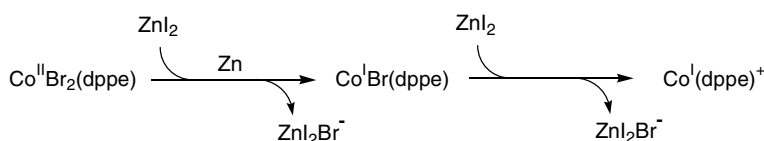
Scheme 2.

Scheme 1.

Table 1
Cobalt(I)-catalyzed dimerisation/trimerisation of phenylacetylene in the absence of a Lewis acid

No.	$CoBr_2(dppe)$ (mol%)	Mg (mol%)	Zn (mol%)	Solvent	Time	Dimer (**1**) (%)	Trimers[c] (%)
1[a]	20	100	–	CH_3CN/CH_2Cl_2[b]	14 h	9	n.i.
2[a]	2	10	–	CH_3CN	20 h	32	49
3	2	10	10	CH_3CN	10 min	36	53
4	2	40	40	CH_3CN	10 min	26	22
5	2	40	10	CH_3CN	10 min	34	49
6	2	10	40	CH_3CN	10 min	34	45
7	2	10	–	CH_3CN	10 min	47	41
8	2	–	40	CH_3CN	10 min	7	8

Reaction conditions: phenylacetylene (2.0 mmol), CH_3CN (1.0 mL), room temperature.
[a] Without previous heating of the catalyst mixture.
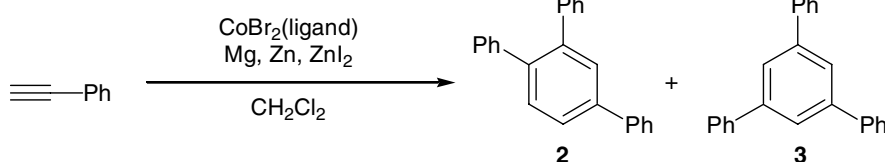[b] CH_2Cl_2 (1.0 mL), CH_3CN (0.1 mL).
[c] The ^1H NMR shows additional olefinic protons. n.i. = not isolated.

2.2. Alkyne trimerisation

In the cobalt-catalysed Diels–Alder reaction of alkynes with 1,3-dienes the use of a Lewis acid such as zinc iodide proved to be essential for the catalytic activity. When zinc iodide was added to the catalyst mixture containing magnesium and zinc as reducing agent, a good conversion of the phenylacetylene into the cyclic trimers **2** and **3** was observed (Scheme 3) [7]. The first experiments were conducted with CoBr₂(dppe) as catalyst precursor in dichloromethane and gave in 70% yield a 4.8:1.0 mixture of **2:3** in a relatively short reaction time at ambient temperatures (Table 2, entry 1).
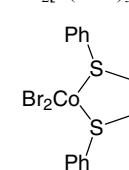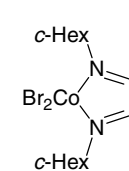
Encouraged by this result obtained with this catalyst system, we subsequently investigated a small number of different ligands on the cyclotrimerisation reaction to identify general trends of the reaction. In all cases, the use of the Lewis acid zinc iodide favoured the formation of the cyclotrimerisation products dramatically, so that only traces of previously observed linear dimerisation or trimerisation products could be found. The use of electron rich ligands such as tricyclohexylphosphine (Table 2, entry 5) turned out to have advantages under the applied reaction conditions, whereas the use of other bidentate or monodentate phosphine ligands (Table 2, entries 1–4 and 6) were contra productive [8]. Although phosphine ligands are among the most prominent and versatile ligands used in transition metal catalysed reactions, other donor based and readily available ligands were tested. Very interesting results were obtained when ethylene diphenylthioether or cyclohexyl diimine complexes (Table 2, entries 7 and 8) were tested [9]. The reaction times shortened dramatically and after complete conversion the isolated yields were excellent (>94%). Particularly, interesting was the observation that the isomeric ratio of the unsymmetrical product (**2**) and the symmetrical product (**3**) is noticeably modified by these different types of ligands. While the symmetrical arene **3** is obtained as main product by the disulfide complex (Table 2, entry 7), the diimine and most phosphine complexes predominantly yield the 1,2,4-substituted product (**2**). Again, a thermal pre-treatment of the system components in solution prior to substrate addition decreases the reaction time drastically.

Phenylacetylene proved to be a good choice as substrate because the ratio of the regioisomereic cyclotrimerisation products 1,2,4-triphenylbenzene (**2**) and 1,3,5-triphenylbenzene (**3**) can be easily determined via

¹H NMR spectroscopy. Although, a large number of phosphine ligands are known, slight modifications of the ligand often result in tedious syntheses accompanied with problems related to the air sensitivity of phosphorus(III) compounds. In contrast, the chemistry of disulfide or diimine ligands is comparably simple and modifications can be easily prepared on a large scale using inexpensive commercially available starting materials.

2.3. Solvent effect on the alkyne trimerisation

Due to an easy synthetic approach to diimines we chose these ligands for our next set of experiments. In the course of our investigations magnesium was found

Table 2
Cobalt(I)-catalyzed [2+2+2]-cyclotrimerisation of phenylacetylene using different ligands

No.	Catalyst precursor	Time (h)	Yield (%)	Ratio **2:3**
1	CoBr₂(dppe)	3	70	4.8:1.0
2	CoBr₂(PPh₃)₂	20[b]	57	5.0:1.0
3	CoBr₂(dppm)[a]	16	8[c]	1.0:1.5
4	CoBr₂(dppf)[a]	20[b]	25[c,d]	–
5	CoBr₂(Pc-Hex₃)₂[a]	16	88	8.3:1.0
6	CoBr₂[P(o-tol)₃]₂[a]	20	Traces	–
7		4	96[e]	1.0:2.9[e]
8		5	94	5.8:1.0

Reaction conditions: phenylacetylene (2.0 mmol), catalyst (5 mol%), magnesium (25 mol%), zinc (10 mol%), zinc iodide (10 mol%), CH₂Cl₂ (1.0 mL), room temperature.
[a] The catalyst was generated in situ.
[b] Incomplete conversion.
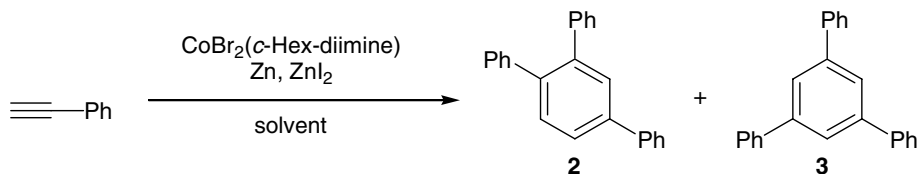[c] The enyne **1** was detected in trace amounts.
[d] The ¹H NMR shows additional olefinic protons, therefore the ratio of regioisomeres can not be evaluated.
[e] The product contained traces of the ligand, so that the yield was corrected by integration of the ¹H NMR spectrum.

Scheme 3.

Scheme 4.

to be not necessary for the generation of the active species to undergo the cyclotrimerisation process. Additionally, the presence of magnesium as reducing agent does not influence the isomeric ratio significantly. Having found a strong ligand dependency on the isomeric ratio we assumed that the ability of solvents to coordinate to the low valent cobalt catalyst might influence the product ratio as well. Therefore, the reaction of phenylacetylene with the bis-cyclohexylethylene diimine cobalt bromide complex (Scheme 4) was performed in various solvents to test this hypothesis.

Indeed, solvent effects on the catalyst system are drastic. An impact on yield, reaction time and isomeric ratio is found. Highly polar or protic solvents such as DMF, DMSO and ethanol gave very low conversions of the starting material, while relatively unpolar solvents such as dibutyl ether or toluene gave no conversion of the starting material based on the low solubility of the catalyst system in these solvents. Among several oxygen containing solvents the most interesting behaviour was observed in THF where a relatively good yield was combined with a shifted regioselectivity slightly favouring the symmetrical isomer. The most intriguing behaviour was, however, observed in acetonitrile as solvent where the addition of the starting material led to a very fast conversion. Surprisingly, in acetonitrile a very short reaction time was accompanied with an excellent regioselectivity in favour of the unsymmetrical product **2**. Further increase of the sterical hindrance of the nitrile (Table 3, entries 18–21) led to somewhat lower reactions rates and a lower selectivity compared to the reaction in acetonitrile. Nevertheless, from a subjective point of view, the reaction in benzonitrile was probably the fastest observed and the most exothermic. However, the regioselectivity was not as distinct as in acetonitrile. Also, the separation of the desired products from benzonitrile was somewhat more difficult. The dependency of the regiochemistry of the products from the solvent used let us speculate that a solvent molecule acts as a ligand on the cobalt centre during the bond formation process. To underline this solvent dependency and a coordination of acetonitrile, the trimerisation reaction was performed in a solvent system consisting of THF and acetonitrile with various mixing ratios (Fig. 1). To 5 mol% of the cobalt catalyst, an increasing number of acetonitrile were added. The result is a very steep decay of the ratio between **2** and **3** starting from pure THF

Table 3
Solvent dependency of the cobalt(I)-catalyzed [2+2+2]-cyclotrimerisation of phenylacetylene

No.	Solvent	Time	Yield (%)	Ratio **2:3**
1	Acetone	5 h	39	3.0:1.0
2	DMSO	15 h	3	30.5:1.0
3	DMF	20 h	Traces	–
4	Ethanol	20 h[a]	7	2.7:1.0
5	EtOAc	15 h	71	4.3:1.0
6	CH_2Cl_2	4 h	94	5.8:1.0
7	$ClCH_2CH_2Cl$	15 h	95	5.3:1.0
8	Et_2O	20 h[a]	26[b]	3.6:1.0
9	Bu_2O	15 h	0	–
10	Dioxane	20 h	32[c]	2.5:1.0
11	THF	12 h[d]	96	1.0:1.3
12	2-Methyl-THF	15 h	81	1.1:1.0
13	Furan	15 h	32	4.5:1.0
14	THP	15 h	81	2.4:1.0
15	$MeOCH_2CH_2OMe$	20 h	60[c]	3.8:1.0
16	Pyridine	20 h	13[c]	19.9:1.0
17	Toluene	20 h[a]	0	–
18	CH_3CN	10 min	99	19.2:1.0
19	EtCN	30 min	95	10.8:1.0
20	t-BuCN	15 h	53	7.1:1.0
21	PhCN	10 min	95	11.8:1.0

Reaction conditions: phenylacetylene (2.0 mmol), cobalt complex (5 mol%), zinc (10 mol%), zinc iodide (10 mol%), solvent (1.0 mL), room temperature.
[a] Incomplete conversion.
[b] The ^{1}H NMR shows additional olefinic protons.
[c] Also 1,4-diphenylbuta-1,3-diyne was isolated in trace amounts (<2%).
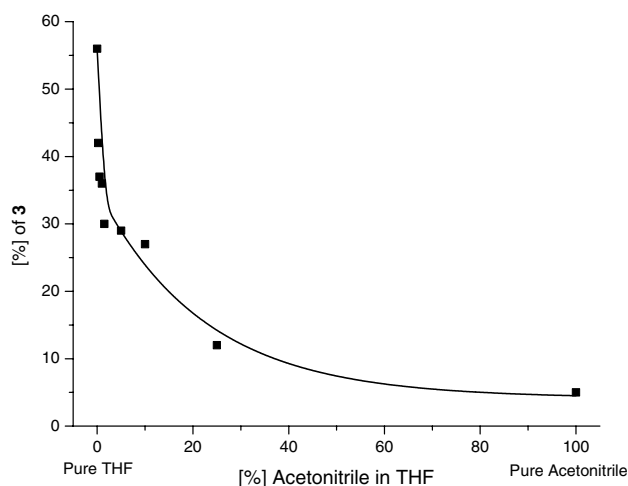[d] Without previous heating of the catalyst mixture.

Fig. 1. Ratio of the symmetrical trimer subject to the composite of the used solvent mixture.

(**2**:**3** = 1.0:1.3) when small amounts of acetonitrile are present. A lesser exponential decay is observed when larger amounts of acetonitrile are added until the reaction in pure acetonitrile gave **2**:**3** in a 19.2:1.0 ratio.

Accordingly, even small amounts of acetonitrile have a profound effect on the regioselectivity and an incorporation of acetonitrile as a ligand can be presumed. Accompanied with this coordination of the nitrile solvent a reorganisation of the ligands at the cobalt centre can be envisaged. However, predictions upon the geometry and the orientations of the ligands within the transition state are highly speculative at this point.

Three solvents were chosen to be most interesting for the next reactions. The reactivity in acetonitrile is outstanding and an excellent ratio in favour of the unsymmetrical product **2** is obtained (Table 3, entry 18). In tetrahydrofurane this ratio is reversed with the diimine cobalt complex (Table 3, entry 11), the same result is obtained with the disulfide complex in dichloromethane (Table 2, entry 7). All three solvents provide good to excellent yields and no traces of olefinic protons, indicating open chain trimers or oligomers.

2.4. Ligand effect on the alkyne trimerisation

For a further increase of the reactivity and regioselectivity as well as for a more comprehensive understanding of the effects induced by the ligand system, the diimine motif was further modified. Subsequently, two cobalt phosphine complexes and several cobalt imine type complexes were tested in acetonitrile, tetrahydrofurane and dichloromethane (see Scheme 5).

An overall trend can be identified from the data summarised in the table: the reactivity of most complexes follows mainly the order $CH_3CN \gg THF > CH_2Cl_2$. Unfortunately, other parameters such as yield and reactivity differ even within a class of complexes. Small changes in the ligand sphere altered the results, so that a general discussion is inappropriate. However, the positive effects of the more electron rich phosphine ligands were also observed in the other tested solvents. Particularly in Table 4, entry 4 the results for the $CoBr_2(Pc\text{-}Hex_3)_2$ complex are excellent regarding the reactivity of the catalyst system, the isolated yield as well as the regioselective formation of the unsymmetrical product. The greatest difference in terms of the regioselectivity
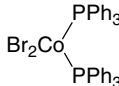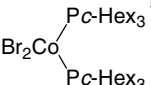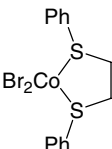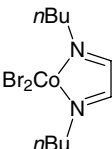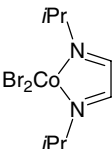
was found for the disulfide complex (Table 4, entries 7–9). While the data for the reaction in acetonitrile are excellent (96%, **2**:**3** = 16.0:1.0), in the weakly coordinating solvent dichloromethane, the regioselectivity was inversed to give the symmetrical product as main isomer (**2**:**3** = 1.0:2.9). The reactivity of the disulfide complex in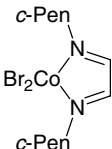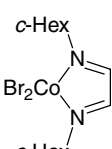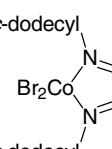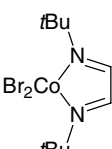 CH_2Cl_2 was higher compared to the reaction conducted in THF. This behaviour is different to the diimine complexes which exhibit a higher reactivity in THF. In these reactions (Table 4, entries 10–33) we found a profound effect of the steric properties on the reactivity and the selectivity of the complexes. A steric increase of the nitrogen-substituents leads to an improvement of the isomeric ratio in acetonitrile in favour of the unsymmetrical product.

While the *n*-butyl diimine complex produces a ratio of **2**:**3** = 7.0:1.0, the ratio is gradually increased with the ligands *iso*-propyl, *cyclo*-pentyl, *cyclo*-hexyl, Mesityl and *tert*-butyl. For the latter t-butyl diimine complex an excellent ratio of 29.0:1.0 is obtained. In principle a decreased reactivity of the complexes is observed when the steric bulk of the ligand is increased. Although all complexes are very reactive, the best combination of yield, reactivity and regioselectivity is obtained with the dicyclohexyl diimine complex (Table 4, entry 19). In contrast to all other diimine ligands tested this particular complex shows a drastic change of the regioselectivity in different solvents. In THF the regioselectivity is changed favouring the symmetrical product **3** (Table 4, entry 21). With the corresponding complex having two additional methyl groups in the backbone of the diimine motif (Table 4, entries 31–33) such a dramatic change of the reaction characteristics was not found. The hypothesis that the conformational flexibility of the cyclohexyl ring could have an influence on the regioselective formation of the intermediates during the cyclotrimerisation processes can not be ruled out with the present set of experiments. Among the other catalyst systems tested we would like to emphasise that also pyridine type ligands (Table 4, entries 37–45) and a tertiary amine ligand (Table 4, entry 49) was compatible with the reaction and gave also promising results. Surprisingly, the reaction can be performed even with $CoBr_2$ in acetonitrile without any additional ligands. The regioisomeric ratio in this case is 18.6:1.0 clearly indicating an important part of this solvent in the mechanism as
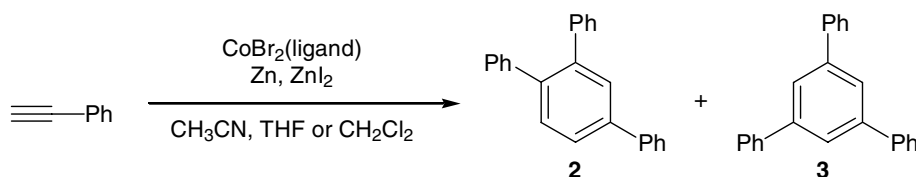
Scheme 5.

Table 4
Cobalt(I)-catalysed [2+2+2]-cyclotrimerisation of phenylacetylene using different ligands in three different solvents

No.	Catalyst precursor	Solvent	Time	Yield (%)	Ratio 2:3
1		CH_3CN	1 h	57	14.3:1.0
2	Br_2Co with PPh_3 ligands	CH_2Cl_2	16 h	66	6.0:1.0
3		THF	16 h	51[b,c]	3.7:1.0
4		CH_3CN	30 min	91	21.8:1.0
5	Br_2Co with $Pc\text{-Hex}_3$[a] ligands	CH_2Cl_2	16 h	88	8.3:1.0
6		THF	16 h	40	3.5:1.0
7		CH_3CN	30 min	96	16.0:1.0
8	Br_2Co with Ph-S,S-Ph dithiolate	CH_2Cl_2	5 h	96[d]	1.0:2.9
9		THF	16 h	42	1.8:1.0
10		CH_3CN	15 min	75	7.0:1.0
11	Br_2Co with nBu diazadiene	CH_2Cl_2	16 h	88	4.5:1.0
12		THF	16 h	58[e]	2.4:1.0
13		CH_3CN	15 min	90	11.9:1.0
14	Br_2Co with iPr diazadiene	CH_2Cl_2	16 h	87	4.6:1.0
15		THF	4 h	69	7.4:1.0
16		CH_3CN	1 h	99	16.4:1.0
17	Br_2Co with c-Pen diazadiene	CH_2Cl_2[g]	15 h	94	2.7:1.0
18		THF	3 h	75	3.4:1.0
19		CH_3CN	10 min	99	19.2:1.0
20	Br_2Co with c-Hex diazadiene	CH_2Cl_2	4 h	94	5.8:1.0
21		THF	12 h	96	1.0:1.3
22		CH_3CN	15 min	93	13.6:1.0
23	Br_2Co with c-dodecyl diazadiene	CH_2Cl_2	16 h	81	4.9:1.0
24		THF	1.5 h	92	16.7:1.0
25		CH_3CN	30 min	90	29.0:1.0
26	Br_2Co with tBu diazadiene	CH_2Cl_2	16 h	81	6.0:1.0
27		THF	16 h	85[c]	13.7:1.0

(*continued on next page*)

Table 4 (continued)
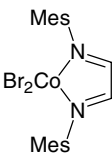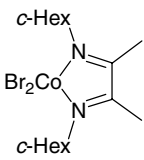
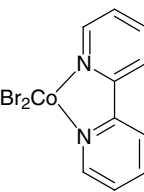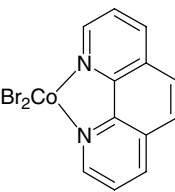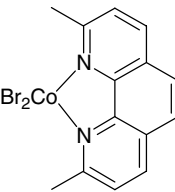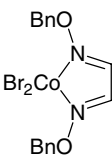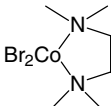| No.	Catalyst precursor	Solvent	Time	Yield (%)	Ratio 2:3
28	Mes / N / Br₂Co / N / Mes	CH₃CN	30 min	85	21.3:1.0
29		CH₂Cl₂	16 h	31	2.6:1.0
30		THF	16 h	22	6.3:1.0
31	c-Hex / N / Br₂Co / N / c-Hex	CH₃CN	30 min	94	21.3:1.0
32		CH₂Cl₂	16 h	75	5.3:1.0
33		THF	16 h	66	5.6:1.0
34	(spiro oxazoline Co complex)	CH₃CN	1 h	99	19.0:1.0
35		CH₂Cl₂	15 h	0	–
36		THF	3 h	36	3.5:1.0
37	(bipyridine) Br₂Co	CH₃CN	1 h	99	31.0:1.0
38		CH₂Cl₂	15 h	92	17.6:1.0
39		THF	3 h	86	9.4:1.0
40	(phenanthroline) Br₂Co	CH₃CN	1 h	99	22.3:1.0
41		CH₂Cl₂	15 h	0	–
42		THF	3 h	99	12.3:1.0
43	(dimethyl phenanthroline) Br₂Co	CH₃CN	1 h	99	21.3:1.0
44		CH₂Cl₂	15 h	37	8.6:1.0
45		THF	3 h	Traces	–
46	BnO / N / Br₂Co / N / BnO	CH₃CN	1.5 h	56	14.9:1.0
47		CH₂Cl₂	10 h	n.i.	–
48		THF	10 h	n.i.	–
49	N / Br₂Co / N	CH₃CN	1 h	99	27.0:1.0
50		CH₂Cl₂	15 h	0	–
51		THF	3 h	Traces	–

Table 4 (continued)

No.	Catalyst precursor	Solvent	Time	Yield (%)	Ratio 2:3
52	CoBr$_2$(salen)	CH$_3$CN	1 h	Traces	–
53		CH$_2$Cl$_2$	15 h	Traces	–
54		THF	3 h	Traces	–
55	CoBr$_2$	CH$_3$CN	30 min	99	18.6:1.0
56		CH$_2$Cl$_2$	16 h	0[f]	–
57		THF	16 h	4	–

Reaction conditions: phenylacetylene (2.0 mmol), cobalt complex (5 mol%), zinc (10 mol%), zinc iodide (10 mol%), solvent (1.0 mL), room temperature.
[a] The catalyst was generated in situ.
[b] In addition the enyne 1 was isolated in 27% yield.
[c] The ^{1}H NMR shows additional olefinic protons.
[d] The product contained traces of the ligand, so that the yield was corrected by integration of the ^{1}H NMR spectrum.
[e] Traces of the enyne 1 were detectable by GC–MS.
[f] When CoBr$_2$(CH$_3$CN)$_x$ was used after 16 h 75%, of the arene were isolated (2:3 = 5.3:1.0).
[g] Without previous heating of the catalyst mixture. n.i. = not isolated, very low conversion.

outlined above in the investigation with different nitrile type solvents. In dichloromethane the poorly soluble anhydrous CoBr$_2$ alone gave no conversion. When anhydrous cobalt bromide was stirred in acetonitrile, the solvent removed an acetonitrile adduct [CoBr$_2$(CH$_3$CN)$_x$] was obtained [10]. This complex was used as a pre-catalyst in dichloromethane to yield 75% of the trimerisation products (2:3 = 5.3:1.0) which were isolated after 16 h reaction time. In THF both, the anhydrous cobalt bromide as well as the [CoBr$_2$(CH$_3$CN)$_x$] gave very low conversions (>5%). These effects also suggest that the active catalyst species in acetonitrile could at least be coordinated partially by a nitrile ligand.

In summary, acetonitrile is the solvent of choice for the formation of the 1,2,4-substituted product. The reactivity in this solvent is extraordinary and the products are isolated in high yields. Additionally, several classes of donor ligands (electron rich phosphines, imines, amines, pyridines and sulfides) can be used to obtain interesting results. Furthermore, a large number of combinations of these substructures could be envisaged and most likely easily be synthesised. However, the not uniform tendencies regarding isomeric ratios and yields in dichloromethane and tetrahydrofurane where the reaction proceeds generally slower can not easily be understood.

## 2.5. Competition experiments and mechanistic aspects

The investigations so far led from a catalyst system consisting of CoBr$_2$(dppe), Zn and ZnI$_2$ in dichloromethane to a system consisting of CoBr$_2$(diimine), Zn, ZnI$_2$ in acetonitrile. While the first catalyst system is well suited to initiate Diels–Alder reactions of non-activated starting materials, the second system seems to be very selective for the cyclotrimerisation of terminal and internal alkynes. From a synthetical point of view, it was also important to show changes in chemoselectivity. Therefore, competition experiments with phenylacetylene and isoprene were conducted. The three reactions in Scheme 6 gave an interesting result, which will be of some relevance when the reaction mechanisms are taken into account [11].

The important observation for the synthetically interested chemist is that the chemoselectivity was indeed strongly altered by changing the ligand and the solvent system. Although, the cyclotrimerisation reaction is performed in acetonitrile no corresponding pyridine derivative could be observed (GC–MS) [12]. The third reaction in Scheme 6 is interesting from a mechanistic point of view because of the formation of the cyclooctatriene derivative 5 by a formal [4+2+2]-cycloaddition process in 31% yield [13,14]. Either the formation of 5 represents an alternative reaction pathway during the cyclotrimerisation reaction, or 5 is formed as a side product in the Diels–Alder reaction. In the first case a reaction of isoprene with a 3,4-diphenyl substituted cobaltacyclopentadiene derivative must be proposed. Such an intermediate is not believed to be of any relevance in the cyclotrimerisation processes investigated thus far [9]. The second possible route for the formation of 5 is the insertion of phenylacetylene into a cobaltacycle intermediate during the formation of the Diels–Alder product (Scheme 7) [15]. From the proposed cobaltacycle intermediate 6 a reductive elimination leads to the Diels–Alder product 4 which was also observed in 64% yield with the para to meta regioselectivity of 4.8:1.0 [3]. Based on the observation that the cyclooctatriene derivative shows a 1,2-diphenyl substitution pattern, one has to conclude, that the insertion process goes via intermediate 6 with a
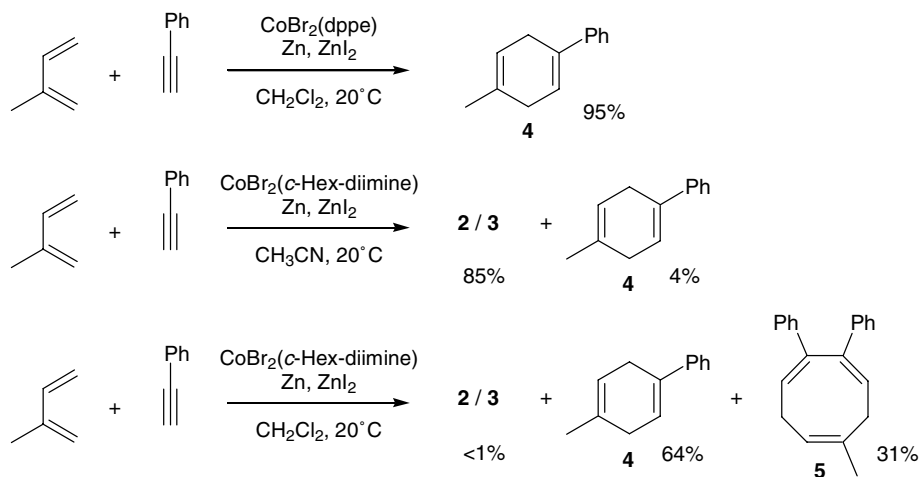
Scheme 6.
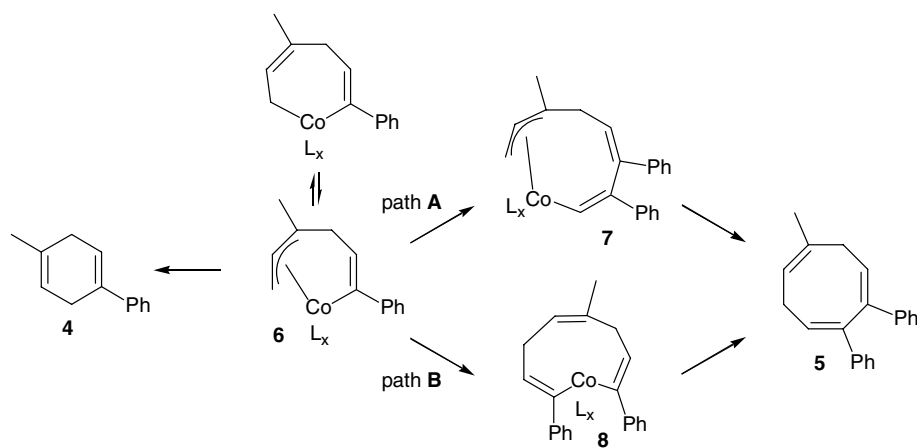
Scheme 7.

phenyl substituent next to the cobalt centre. From this species, the formation of the cyclooctatriene **5** has to proceed by an insertion either in the vinyl-cobalt bond (path A) via **7** or into the allylic substructure on the side of the isoprene (path B) via **8**. The formation of **5** can be rationalised by reductive elimination from the intermediates **7** and **8**. At this point we are not able to differentiate whether path A or path B is the more favourable reaction pathway.

For the cyclotrimerisation process and the effects observed in different nitrile type solvents, effects based on sterically modifications on the diimine ligands as well as the regioselectivity changes in the three tested solvents CH_3CN, CH_2Cl_2 and THF one can speculate that a solvent molecule could be present in the ligand sphere during the reaction pathway. A definite interpretation of the data or a plausible unifying transition state model explaining all observed effects can not be given at the present time.

3. Summary

Within this investigation, we were able to show that additives influenced the reactivity of cobalt phosphine and cobalt diimine type complexes dramatically. Firstly, the dimerisation process of phenylacetylene can be catalysed in acceptable yields with $CoBr_2(dppe)$ as catalyst precursor using magnesium as reducing agent. Secondly, the addition of a Lewis acid and the substitution of magnesium towards zinc as reducing agent favoured the cyclotrimerisation reaction of phenylacetylene in acetonitrile. The best results for the cyclotrimerisation towards the unsymmetrical product **2** were obtained for diimine type ligands. In contrast, when diphenylethylene disulfide was used as ligand the regioselectivity was inversed and the symmetric trimer **3** is obtained as major product. Diimine cobalt complexes gave excellent results in acetonitrile as solvent. Furthermore, the investigation showed that the solvent has a profound effect which can only be

rationalised when a coordination of the nitrile is assumed in the transition state. Thirdly, the chemoselectivity of the complexes could be demonstrated in competition experiments where either the Diels–Alder product **4** or the cyclotrimerisation product **5** was formed predominantly. The competition experiment in dichloromethane led to the formation of an unprecedented [4+2+2]-cyclisation product. The regiochemistry of this cyclooctatriene derivative **5** gave a valuable insight into the regioselective formation of the intermediate in the cobalt catalysed Diels–Alder reaction.

4. Experimental

4.1. General information

All manipulations were carried out using standard Schlenk techniques under an atmosphere of argon or nitrogen. All solvents for use in an inert atmosphere were purified by standard procedures and distilled under nitrogen immediately prior to use. Other chemicals were obtained from commercial sources and used without further purification. ^1H and ^{13}C NMR spectra were recorded on Bruker Physics ARX 300 and Bruker Physics ARX 400 spectrometer in $CDCl_3$. The spectra are calibrated to the residual protons of the solvent (^1H) or to the 13-carbon signals of the solvent (^{13}C). Mass spectra were recorded on a Varian MAT CH 7a, a Finnigan MAT 95S or a Micromass VG AutoSpec spectrometer.

4.2. Synthesis of diimine complexes

The ligands were synthesised as previously described in the literature or by adapting known procedures [16]. The complexes were synthesised by suspending anhydrous $CoBr_2$ (2.18 g, 10.0 mmol) and the ligand (10.0 mmol) in anhydrous THF (40 mL) at room temperature [17]. After stirring overnight the solvent was removed in vacuo and the solid product was used without further purification.

4.3. Representative procedure for the di- and trimerisation reaction

A suspension of $CoBr_2$(dppe) (62 mg, 0.1 mmol, 5.0 mol%), zinc dust and magnesium chips in anhydrous CH_3CN (1.0 mL) under argon atmosphere was shortly heated to reflux, allowed to cool to room temperature and stirred for 30 min. The reactions without zinc dust were again shortly heated to reflux, allowed to cool to room temperature and stirred for additional 30 min. Phenylacetylene (0.22 mL, 2.0 mmol) was added to the brown suspension and the mixture stirred at room temperature for 10 min. The brown reaction mixture was passed through a pad of silica using CH_2Cl_2 as eluent. The solvents were removed and the crude product puri-

fied by flash chromatography using pentane/CH_2Cl_2 100:1 as eluent. (*E*)-1,4-Diphenyl-but-1-en-3-yne (**1**) and an inseparable mixture of cyclic and acyclic trimers of phenylacetylene were isolated. The spectral data of the products isolated in pure form are consistent with the literature [5].

4.4. Representative procedure for the cyclotrimerisation reaction

A suspension of the cobalt complex (0.1 mmol, 5.0 mol%), zinc dust (13 mg, 0.2 mmol, 10.0 mol%) and anhydrous ZnI_2 (64 mg, 0.2 mmol, 10.0 mol%) in anhydrous solvent (CH_3CN, CH_2Cl_2 or THF) (1.0 mL) under argon atmosphere was shortly heated to reflux and allowed to cool to room temperature. After 15 min phenylacetylene (0.22 mL, 2.0 mmol) was added and the mixture stirred at room temperature. The reaction was monitored by thin layer chromatography. After complete conversion the brown reaction mixture was passed through a pad of silica using CH_2Cl_2 as eluent. The solvents were removed and the crude product purified by flash chromatography using pentane/CH_2Cl_2 100:1 as eluent. The ratio of regioisomeres **2**:**3** was verified by integration of the ^1H NMR.

4.5. Competition experiments

Following the general procedure for the trimerisation reactions, bis-cyclohexyliden ethane diimine cobalt dibromide (44 mg, 0.1 mmol, 5.0 mol%), zinc dust (13 mg, 0.2 mmol, 10.0 mol%) and anhydrous zinc iodide (64 mg, 0.2 mmol, 10.0 mol%) were suspended in dry solvent (1.0 mL) under argon atmosphere, shortly heated to reflux and allowed to cool to room temperature. After 15 min isoprene (0.24 mL, 2.4 mmol) and phenylacetylene (0.22 mL, 2.0 mmol) were added and the mixture stirred at room temperature. The reaction was monitored by thin layer chromatography (CH_3CN 0.5 h, CH_2Cl_2 5.5 h, THF 5.0 h). After complete conversion the brown reaction mixture was passed through a pad of silica using CH_2Cl_2 as eluent. The solvents were removed and the crude product was purified by flash chromatography using pentane/CH_2Cl_2 100:1 as eluent.

(1*Z*,3*Z*,6*Z*)-6-Methyl-2,3-diphenyl-cycloocta-1,3,6-trien (**5**): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.43 (dt, 4 H, *J* = 7.2, 1.2 Hz), 7.29 (t, 4 H, *J* = 7.5 Hz), 7.22 (dt, 2 H, *J* = 7.3, 1.2 Hz), 6.24 (t, 1 H, *J* = 7.8 Hz), 6.20 (t, 1 H, *J* = 7.8 Hz), 5.56 (tq, 1 H, *J* = 6.0, 1.2 Hz), 2.87 (bs, 4 H), 1.87 (d, 3 H, *J* = 1.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.1, 140.6, 138.9, 135.1, 128.4, 127.1, 127.0, 126.8, 126.7, 123.9, 123.4, 120.2, 34.0, 28.3, 27.3. MS (EI): *m/z* = 272 (47, M$^+$), 257 (23), 244 (100), 229 (51), 217 (24), 202 (14), 178 (17), 165 (23), 115 (19), 91 (17). HRMS calculated for $C_{21}H_{20}$: *m/z* = 272.1565, found: *m/z* = 272.1559.

Acknowledgements

References

[1] For reviews see: M. Malacria, C. Aubert, J.L. Renaud, in: M. Lautens, B.M. Trost (Eds.), Science of Synthesis: Houben–Weyl Methods of Molecular Transformations, vol. 1, Thieme, Stuttgart, 2001, pp. 439–530;
S. Saito, Y. Yamamoto, Chem. Rev. 100 (2000) 2901;
I. Ojima, M. Tzamarioudaki, Z. Li, R.J. Donovan, Chem. Rev. 96 (1996) 635;
M. Lautens, W. Klute, W. Tam, Chem. Rev. 96 (1996) 49;
D.B. Grotjahn, in: E.W. Abel, F.G.A. Stone, G. Wilkinson, L. Hegedus (Eds.), Comprehensive organometallic chemistry II, vol. 12, Pergamon Press, Oxford, 1995, pp. 741–770;
N.E. Schore, in: B.M. Trost, I. Fleming, L.A. Paquette (Eds.), Comprehensive organic synthesis, vol. 5, Pergamon Press, Oxford, 1991, pp. 1129–1162;
K.P.C. Vollhardt, Angew. Chem. 96 (1984) 525;
K.P.C. Vollhardt, Angew. Chem. Int. Ed. 23 (1984) 539;
For recent examples of cobalt catalysed cyclotrimerisations of alkynes see: L. Yong, H. Butenschön, Chem. Commun. (2002) 2852;
T. Sugihara, A. Wakabayashi, Y. Nagai, H. Takao, H. Imagawa, M. Nishizawa, Chem. Commun. (2002) 576;
M.S. Sigman, A.W. Fatland, B.E. Eaton, J. Am. Chem. Soc. 120 (1998) 5130.
[2] For leading references see: G. Hilt, S. Lüers, K.I. Smolko, Org. Lett. 7 (2005) 251;
G. Hilt, S. Lüers, K. Harms, J. Org. Chem. 69 (2004) 624;
G. Hilt, K.I. Smolko, Angew. Chem. 115 (2003) 2901;
G. Hilt, K.I. Smolko, Angew. Chem. Int. Ed. 42 (2003) 2795.
[3] G. Hilt, F.-X. du Mesnil, Tetrahedron Lett. 41 (2000) 6757.
[4] H. Brunner, A. Reimer, Bull. Chem. Soc. Fr. 134 (1997) 307;
M. Lautens, W. Tam, J.C. Lautens, L.G. Edwards, C.M. Crudden, A.C. Smith, J. Am. Chem. Soc. 117 (1995) 6863;
O. Pardigon, A. Tenaglia, G. Buono, J. Org. Chem. 60 (1995) 1868;
O. Pardigon, G. Buono, Tetrahedron: Asymmetry 4 (1993) 1977;
I.-F. Duan, C.-H. Cheng, J.-S. Shaw, S.-S. Cheng, K.F. Liou, J. Chem. Soc., Chem. Commun. (1991) 1347.
[5] Other phosphine ligands were not tested; compare [6].
[6] For dimerisation processes of alkynes see: K. Komeyama, K. Takehira, K. Takaki, Synthesis (2004) 1062;
L.D. Field, A.J. Ward, J. Organomet. Chem. 681 (2003) 91;
A.M. Trzeciak, J.J. Ziółkowski, Pol. J. Chem. 77 (2003) 749;
S. Pasynkiewicz, A. Pietrzykowski, E. Olędzka, J. Wang, Pol. J. Chem. 77 (2003) 701;
W.A. Herrmann, V.P.W. Bohm, C.W.K. Gstottmayr, M. Grosche, C.-P. Reisinger, T. Weskamp, J. Organomet. Chem. 617 (2001) 616;
L.D. Field, A.J. Ward, P. Turner, Aust. J. Chem. 52 (1999) 1085;
H.-Y. Rhyoo, B.Y. Lee, H.K.B. Yu, Y.K. Chung, J. Mol. Catal. 92 (1994) 41;
R. Herrmann, A.J.L. Pombeiro, Monatsh. Chem. 119 (1988) 583.
[7] G. Hilt, T. Vogler, W. Hess, F. Galbiati, Chem. Commun. (2005) 1474;
M.-S. Wu, M. Shanmugasundaram, C.-H. Cheng, Chem. Commun. (2003) 718.

[8] M.-S. Wu, D.K. Rayabarapu, C.-H. Cheng, Tetrahedron 60 (2004) 10005;
P. Turek, M. Kotora, I. Tišlerová, K. Hocek, I. Votruba, I. Císařová, J. Org. Chem. 69 (2004) 9224;
L. Dufková, I. Císařová, P. Štepnička, M. Kotora, Eur. J. Org. Chem. (2003) 2882;
F. Slowinski, C. Aubert, M. Malacria, Adv. Synth. Catal. 343 (2001) 64.
[9] For the synthesis of the cobalt complexes see: M.C. Barral, E. Delgado, E. Gutiérrez-Puebla, R. Jimenez-Aparicio, A. Monge, C. del Pino, A. Santos, Inorg. Chim. Acta 74 (1983) 101;
M.J. Camazón, A. Alvarez-Valdés, J.R. Masaguer, M.C. Navarro-Ranninger, Transition Met. Chem. 11 (1986) 334;
T.V. Laine, M. Klinga, A. Maaninen, E. Aitola, M. Leskelä, Acta Chem. Scand. 53 (1999) 968.
[10] J.J. Banewicz, J.A. Maguire, P.O. Smith, D. Lussky, D.W. Sudbrink, D.E. Allen, J. Chem. Thermodyn. 13 (1981) 629;
V. Gutmann, O. Bohunovsky, Monatsh. Chem. 99 (1968) 740;
B.J. Hathaway, D.G. Holah, J. Chem. Soc. (1964) 2400.
[11] For the reaction mechanism of cyclotrimerisation reactions see: N.E. Schore, Chem. Rev. 88 (1988) 1081;
K.P.C. Vollhardt, Angew. Chem. 96 (1984) 525;
K.P.C. Vollhardt, Angew. Chem. Int. Ed. 23 (1984) 539;
H. Bönnemann, Angew. Chem. 90 (1978) 517;
H. Bönnemann, Angew. Chem Int. Ed. 17 (1978) 525;
H. Yamazaki, Y. Wakatsuki, J. Organomet. Chem. 139 (1977) 157.
[12] H. Bönnemann, Angew. Chem. 97 (1985) 264;
H. Bönnemann, Angew. Chem. Int. Ed. 24 (1985) 248;
H. Bönnemann, W. Brijoux, in: A.R. Katritzky (Ed.), Advances in Heterocyclic Chemistry, vol. 48, Academic Press, San Diego, 1990, pp. 177–222;
L.V.R. Boñaga, H.-C. Zhang, B.E. Maryanoff, Chem. Commun. (2004) 2394;
L.V.R. Boñaga, H.-C. Zhang, D.A. Gauthier, I. Reddy, B.E. Maryanoff, Org. Lett. 5 (2003) 4537;
J.A. Varela, L. Castedo, M. Maestro, J. Mahía, C. Saá, Chem. Eur. J. 7 (2001) 5203;
G.P. Chiusoli, M. Costa, Z. Zhou, Gazz. Chim. Ital. 122 (1992) 441.
[13] Investigations for the expansion of the [4+2+2] cycloaddition reaction to other 1,3-dienes and alkynes are underway.
[14] P.A. Evans, E.W. Baum, A.N. Fazal, M. Pink, Chem. Commun. (2005) 63;
B. Ma, J.K. Snyder, Organometallics 21 (2002) 4688;
S.R. Gilbertson, B. DeBoef, J. Am. Chem. Soc. 124 (2002) 8784;
P.A. Evans, J.E. Robinson, E.W. Baum, A.N. Fazal, J. Am. Chem. Soc. 124 (2002) 8782;
Correction: P.A. Evans, J.E. Robinson, E.W. Baum, A.N. Fazal, J. Am. Chem. Soc. 125 (2003) 14648;
Y. Chen, J.K. Snyder, J. Org. Chem. 63 (1998) 2060;
A. Greco, A. Carbonaro, G. Dall'Asta, J. Org. Chem. 35 (1970) 271.
[15] For the mechanism of the cobalt catalysed cycloaddition reactions see also: M.-S. Wu, D.K. Rayabarapu, C.-H. Cheng, Tetrahedron 60 (2004) 10005;
O. Pardigon, A. Tenaglia, G. Buono, J. Mol. Catal. A 196 (2003) 157;
B. Ma, J.K. Snyder, Organometallics 21 (2002) 4688;
M. Lautens, W. Tam, J.C. Lautens, L.G. Edwards, C.M. Crudden, A.C. Smith, J. Am. Chem. Soc. 117 (1995) 6863, The cyclooctatriene product 5 could not be observed when CoBr₂(dppe) was used as catalyst precursor in dichloromethane

during our investigations on the cobalt catalysed Diels–Alder reactions of non-activated starting materials [2], not even in traces when an excess of the alkyne was used.

[16] G.A. Grasa, M.S. Viciu, J. Huang, S.P. Nolan, J. Org. Chem. 66 (2001) 7729;
M. Haaf, A. Schmiedl, T.A. Schmedake, D.R. Powell, A.J. Millevolte, M. Denk, R. West, J. Am. Chem. Soc. 120 (1998) 12714;

A. Alexakis, N. Lensen, J.-P. Tranchier, P. Mangeney, J. Feneau-Dupont, J.P. Declercq, Synthesis (1995) 1038;
N. De Kimpe, L. D'Hondt, E. Stanoeva, Tetrahedron Lett. 32 (1991) 3879;
J.M. Kliegman, R.K. Barnes, Tetrahedron 26 (1970) 2555.
[17] M.C. Barral, E. Delgado, E. Gutierrez-Puebla, R. Jimenez-Aparicio, A. Monge, C. Del Pino, A. Santos, Inorg. Chim. Acta 74 (1983) 101.