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LETTERS

An improved cobalt catalyst for homo Diels–Alder reactions of acyclic 1,3-dienes with alkynes[†]

Gerhard Hilt* and François-Xavier du Mesnil

Department Chemie, Ludwig-Maximilians Universität München, Butenandtstr. 5-13, 81377 München, Germany

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Abstract

An efficient cobalt(I)-catalysed homo Diels–Alder reaction of acyclic 1,3-dienes and acetylene derivatives is described. The catalyst system consists of a mixture of a readily available $CoBr_2$(dppe) complex, zinc iodide as a cocatalyst, and tetrabutylammonium borohydride as reducing agent. This system increases the reactivity of the cobalt(I) catalyst, so that acyclic dienes and acetylenes can be transformed to the 1,4-dihydroaromatic products in good yield and excellent purity. The regioselectivity of the homo Diels–Alder reaction greatly favours the 1,4-substitution pattern of the formed product. © 2000 Elsevier Science Ltd. All rights reserved.

The usefulness of the Diels–Alder reaction in complexity increasing transformation has been well-established in organic synthesis. While two new carbon–carbon bonds are formed, the regiochemistry and stereochemistry of the cycloaddition can well be controlled and predicted.[1] These statements are especially true for reactions where the two starting materials have different electronical properties. Problems arise when substrates of equal electronic behaviour (homo Diels–Alder reaction), and without the functionality to incorporate a Lewis acid activation, are chosen. In these cases, drastic reaction conditions must be applied and quite often polymerisation is an accompanying side reaction.[2]

The known cobalt(I)-catalysed homo Diels–Alder reactions are mostly limited towards the cycloaddition between 2,5-norbornadiene and acetylene derivatives. The reactive cobalt(I) catalyst is generated in situ from readily available cobalt(II) ($CoI_2/PR_3/Zn$)[3] or cobalt(III) precursors ($Co(acac)_3/PR_3/Et_2AlCl$).[4]

In an attempt to generate a more reactive system starting from cobalt(II) iodide, we have substituted zinc as a reducing agent towards other single electron sources or hydride donors for

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* Corresponding author. Fax: +49 89 21807425; e-mail: gerhard.hilt@cup.uni-muenchen.de

[†] In memoriam Professor Eberhard Steckhan.

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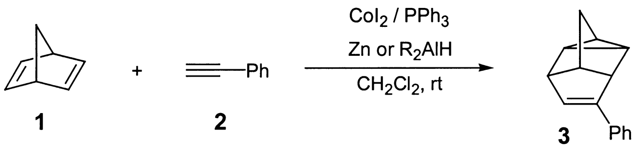
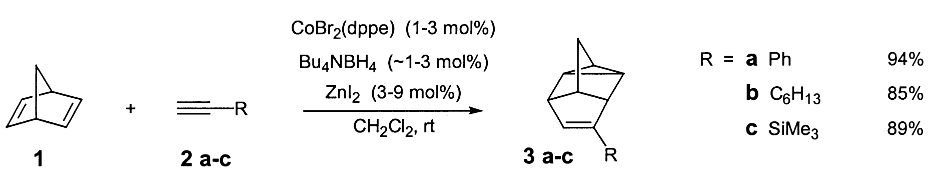
the cycloaddition between 2,5-norbornadiene (**1**) and phenylacetylene (**2**) (Scheme 1). Reducing agents such as manganese, Devarda reagent, lithium naphthalenide, electrochemical reduction (carbon electrode), borohydrides, and aluminium hydrides were used, but to our surprise, even for prolonged reaction times, no or little product could be detected and only in the cases where the original elemental zinc or alanes (DIBAL) were used could the desired product be isolated in reasonable yields.



Scheme 1.

We therefore assumed that the addition of a Lewis acid as a cocatalyst to the reaction mixture might be useful. When zinc iodide was used as an additive, the reaction of **1** and **2** proceeded smoothly with lithium triethoxyaluminiumhydride ($LiAlH(OEt)_3$) or sodium borohydride ($NaBH_4$) as reducing agent. In addition, even cobalt bromide and cobalt chloride triphenylphosphine complexes, unreactive under the original conditions, catalysed the cycloaddition between **1** and **2** after the addition of several equivalents of zinc iodide.

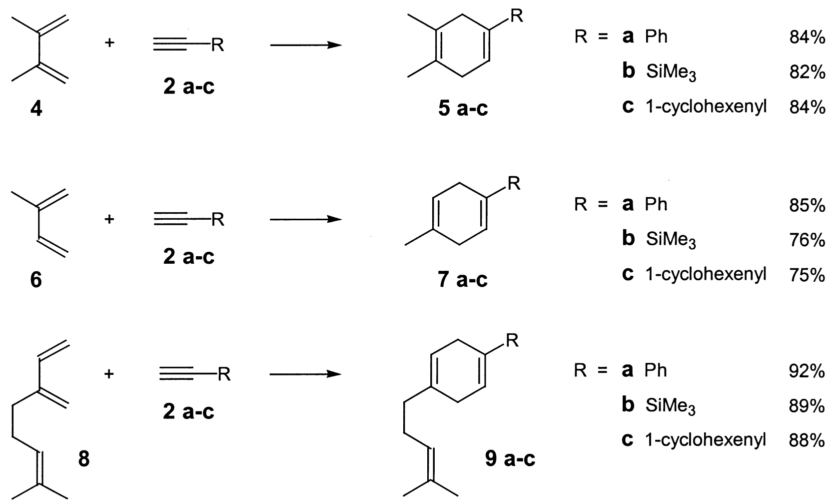
In a series of reactions with different ratios of zinc iodide and the cobalt(II) complex, it was found that the best results were obtained in the presence of 3.0 mol equivalents of ZnI_2, while at higher catalysts to the zinc iodide ratios no further increase in reactivity was observed. The reaction also showed an induction phase (colour changed from green towards a brown solution) whose length was dependent on the reducing agent used. While zinc had a somewhat long induction period, the colour change was observed within minutes for lithium triethoxy aluminiumhydride and immediately for tetrabutylammonium borohydride (Bu_4NBH_4), which is the best soluble reducing agent in dichloromethane used in this series of experiments. We therefore chose a system consisting of $CoBr_2$(dppe), ZnI_2, and Bu_4NBH_4 as a catalyst mixture for homo Diels–Alder reactions. As expected, the reaction of **1** with various alkynes was successfully catalysed by our catalyst system and the products could be obtained in comparable good yields and purities (Scheme 2).[4]



Scheme 2.

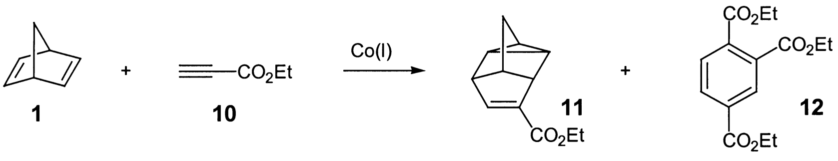
Conversely, the homo Diels–Alder reaction failed for other cyclic 1,3- and 1,4-dienes (such as 1,3-and 1,4-cyclohexadiene, 1,3- and 1,5-cyclooctadiene) with **2a** as dienophile. Such reactions are to our knowledge also not described for the original catalyst systems ($CoI_2/PR_3/Zn$) and ($Co(acac)_3/PR_3/Et_2AlCl$). However, the reaction of acyclic 1,3-dienes like 2,3-dimethyl-1,3-butadiene, isoprene, and myrcene with various terminal alkynes proceeded smoothly to form the corresponding dihydroaromatic systems in >90% conversion (GC-control). Although the products were quite sensitive towards oxidation, difficult to isolate and purify via repeated column chromatography on silica gel with pentane as eluent (especially when myrcene and/or trimethylsilylacetylene are used as starting materials) we were able to isolate the products in good yields and in good GC purity (generally >95%).

The products of the homo Diels–Alder reaction can easily be oxidised by air, so that the corresponding aromatic derivatives are obtained. Thereby the high degree of 1,4- over 1,3-selectivity (generally >15:1) in the cases of isoprene derivatives as diene and terminal acetylenes as dienophile can be established (Scheme 3).



Scheme 3. Reaction conditions: $CoBr_2(dppe)$ (40 mg), ZnI_2 (63 mg), Bu_4NBH_4 (15–17 mg), CH_2Cl_2 (2.0 mL), diene (0.5 mL), alkyne (0.5 mL), ambient temperature, 12–16 h[5]

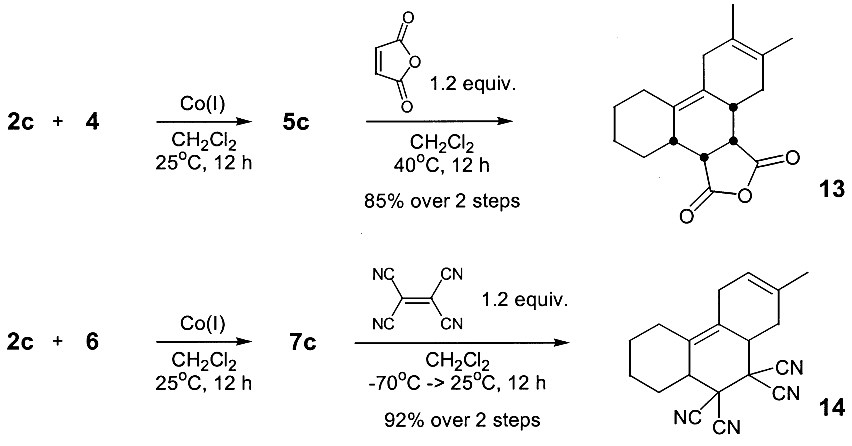
When activated alkynes (ethyl propiolate) and activated alkenes (acrylonitrile) were used as dienophiles precipitates of polymeric nature formed after a short period of time and after complete conversion of the dienophile only traces of the desired product could be detected by GCMS. For example, in the case of the reaction of **1** with ethyl propiolate 5% of the desired homo Diels–Alder product **11** could be isolated as well as 36% of the trimerised 1,2,4-trisubstituted ester **12** and traces of the 1,3,5-substituted triester (Scheme 4).[6]



Scheme 4.

Therefore, the starting material, as in the case of acrylonitrile, is most probably polymerised and could not be detected by GC or isolated after column chromatography.

We then turned our attention towards the possibility of tandem Diels–Alder reactions, since the reaction of 1-ethynyl-cyclohexene (**2c**) with a 1,3-diene under these circumstances provided a new 1,3-diene substructure which could be trapped with reactive dienophiles like tetracyanoethylene or maleic anhydride. Such a tandem Diels–Alder reaction generated polyfunctionalised polycyclic compounds **13** and **14** in good yield, high purity and excellent regiochemistry, which were also much more stable than the dihydroaromatic intermediates and with the polar substituents much easier to purify by chromatography (SiO_2/pentane:$Et_2O = 2:1$ for **13** and diethyl ether for **14**) (Scheme 5).[7]



Scheme 5.

We are currently investigating the possibility of using our catalyst system in combination with a tandem Diels–Alder reaction or other functional group transformation to prepare polyfunctionalised polycyclic precursors for natural product synthesis.

Acknowledgements

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5. Representative procedure for the homo Diels–Alder reaction: In a 50 mL round-bottomed flask under nitrogen, $CoBr_2$(dppe) (40 mg, 64.8 μmol), and ZnI_2 (63. mg, 197.4 μmol) were suspended in dry dichloromethane (2.0 mL) and 2,3-dimethyl-1,3-butadiene (0.5 mL, 363 mg, 4.42 mmol) and phenylacetylene (0.5 mL, 465 mg, 4.55 mmol) were added. To this green mixture 15–17 mg of Bu_4NBH_4 were added until the colour changed to a light brown and the reaction mixture was stirred at ambient temperature for 12 h. After addition of pentane (5 mL), the mixture was filtered through a small amount of silica gel and the solvents evaporated. The product (684 mg, 3.71 mmol, 84%) was obtained as a colourless oil after column chromatography on silica gel with pentane as eluent.
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