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A Concise Synthesis of Substituted Stilbenes and Styrenes from Propargylic Phosphonium Salts by a Cobalt-Catalyzed Diels−Alder/Wittig Olefination Reaction Sequence

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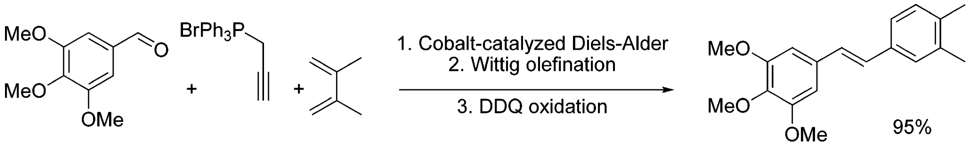

The cobalt(I)-catalyzed Diels−Alder reaction of propargylic phosphonium salts and longer chained alkyne-functionalized phosphonium salts with 1,3-dienes led to dihydroaromatic phosphonium salt intermediates which were directly used in a one-pot Wittig-type olefination reaction with aldehydes. Subsequent oxidation led to styrene- and stilbene-type products under formation of three new carbon−carbon bonds in a single synthetical step starting from three variable starting materials. The *E*/*Z* stereoselectivities of the products revealed that the dihydroaromatic phosphonium ylides behave as semistabilized ylides giving predominantly the *E*-configured products. The application of unsymmetrical 1,3-dienes as well as internal phosphonium functionalized alkynes is also described.

Introduction

The combination of powerful synthetic methods in subsequent one-pot reaction sequences provides a variable access toward a broad variety of products with greatly increased complexity, which incorporate at least three starting materials in a single synthetic transformation. Such processes belong to the classes of intermolecular domino, tandem, and cascade reactions which find broad applications in organic synthesis of complex structures.[1] Among such very well-established reactions are the Diels−Alder cyclooaddition as well as the Wittig olefination. Under these circumstances, some examples are described where an electron-deficient dienophile is generated via a Wittig reaction with a consequent Diels−Alder cyclization reaction.[2] An inverse reaction sequence where an unsaturated phosphonium salt undergoes a thermally induced or transition metal catalyzed cycloaddition process to produce an in situ generated Wittig reagent has not been described thus far to the best of our knowledge.

Under these circumstances, the generation of functionalized dihydroaromatic compounds by means of a cobalt-catalyzed Diels−Alder reaction of nonactivated 1,3-dienes and nonactivated alkynyl type dienophiles has long been a focus of our research. Several functionalized building blocks could be used in this transition metal catalyzed process containing boron-, silicon-, nitrogen-, phosphorus-, oxygen-, and sulfur-functionalized 1,3-dienes or accordingly functionalized alkynes.[3] In addition, several valuable follow-up functionalizations and modifications of the primarily formed dihydroaromatic compounds could be carried out for the synthesis of numerous highly functionalized products.[3d,4]

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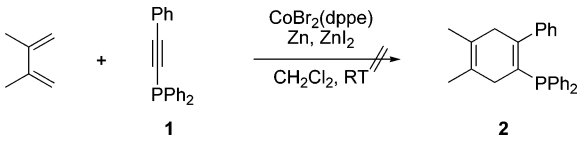
[1] For selected recent reviews, see: (a) Tietze, L. F.; Brasche, G.; Gericke, K. M. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2006. (b) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem.* **2006**, *118*, 7292; *Angew. Chem., Int. Ed.* **2006**, *45*, 7134. (c) Enders, D.; Grondal, C.; Huttl, H. R. M. *Angew. Chem.* **2007**, *119*, 1590; *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (d) Chapman, C. J.; Frost, C. G. *Synthesis* **2007**, 1. (e) Malacria, M. *Chem. Rev.* **1996**, *96*, 289. (f) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (g) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167. (h) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195. (i) Denmark, S. E.; Thorarensen, A. *Chem. Rev.* **1996**, *96*, 137. (j) Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001. (k) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831. (l) Ho, T.-L. *Tandem Organic Reactions*; Wiley-Interscience: New York ,1992. (m) Hall, N. *Science* **1994**, *266*, 32. (n) Tietze, L. F.; Beifuss, U. *Angew. Chem.* **1993**, *105*, 137; *Angew. Chem., Int. Ed.* **1993**, *32*, 131.

[2] Ramachary, D. B.; Barbas, C. F., III. *Chem. Eur. J.* **2004**, *10*, 5323.

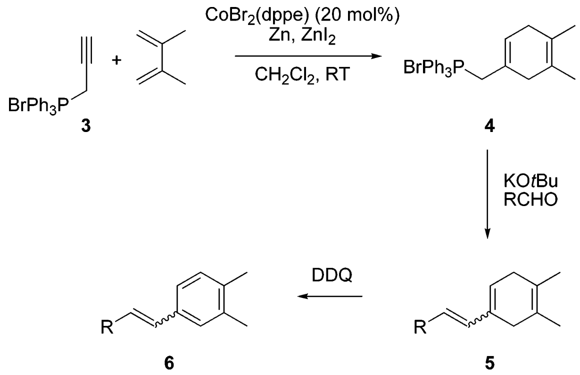
[3] For functionalized building blocks, see the following. Boron: (a) Hilt, G.; Smolko, K. I. *Angew. Chem.* **2003**, *115*, 2901; *Angew. Chem., Int. Ed.* **2003**, *42*, 2795. Silicon: (b) Hilt, G.; Smolko, K. I. *Synthesis* **2002**, 686. Nitrogen: (c) Hilt, G.; Galbiati, F. *Synlett* **2005**, 829. Phosphorus: (d) Hilt, G.; Hengst, C. *Synlett* **2006**, 3247. Oxygen: (e) Hilt, G.; Smolko, K. I.; Lotsch, B. V. *Synlett* **2002**, 1081. Sulfur: (f) Hilt, G.; Lüers, S.; Harms, K. *J. Org. Chem.* **2004**, *69*, 624.

10.1021/jo701406d CCC: $37.00

SCHEME 1



SCHEME 2



Results and Discussion

In an attempt to apply phosphorus-containing starting materials to the arsenal of building blocks suitable for cobalt-catalyzed Diels–Alder reactions, we investigated alkynylphosphines[5] and propargylic phosphonium salts as well as longer chained alkyne-functionalized phosphonium salts as dienophiles in the cobalt-catalyzed cycloaddition process.

First, we investigated the use of an alkynylphosphine derivative (**1**) in the cobalt-catalyzed Diels–Alder reaction with a simple symmetrical 1,3-diene such as 2,3-dimethyl-1,3-butadiene (Scheme 1).

Unfortunately, we have not been able to identify an appropriate cobalt catalyst system which is able to convert starting materials of type **1** into a dihydroaromatic phosphine derivative **2**. The low conversion of the alkynylphosphine **1** is most likely based on a competitive complexation of the phosphorus donor functionality versus the alkynyl moiety. The stronger Co–P coordination of starting material **1** blocks free coordination sites at the cobalt center so that the coordination of the alkyne or the 1,3-diene is less favorable. These results are also in accordance with previous observations namely that the addition of excess phosphine ligand reduces the reactivity of the cobalt catalyst system considerably. Therefore, the complexation of a large excess of the starting material results in an efficient retardation of activity of the cobalt catalyst. Even if the catalysts were applied in up to 50 mol % the desired products will not be obtained.[6]

Nevertheless, the use of propargylic phosphonium salts, such as **3**, was performed because in this type of starting material the phosphorus does not behave as a donor ligand anymore. In addition, this type of transformation seems to be of considerably higher synthetic value in terms of the possibilities implied in the allylic phosponium salt for further carbon–carbon bond formation processes. While the follow-up chemistry of cycloadducts of type **2** is rather limited, the cycloadduct of type **4** should allow a sequential Diels–Alder/Wittig reaction cascade. The proposed cobalt-catalyzed Diels–Alder reaction of a propargylic phosphonium salt such as **3** (Scheme 2) generates a new kind of an allylic-type phosphonium salt **4** with a dihydroaromatic subunit next to the acidic CH-protons suitable for an in situ Wittig olefination with carbonyl compounds such as aldehydes.

If propargylic phosphonium salts such as **3** are brought to reaction in a cobalt-catalyzed Diels–Alder reaction with 1,3-dienes, a systematic problem arises. Not only the starting materials but also the proposed dihydroaromatic intermediates **4** are saltlike intermediates. Therefore, the isolation of phosphonium salt **4** from all the other cobalt and zinc inorganic-type ingredients in the reaction mixture is very tedious. In fact, the phosphonium salt **4** could not be obtained in pure form by recrystallization, filtration, or precipitation. In addition, because of the presence of paramagnetic cobalt catalyst components in the reaction mixture the conversion could not be determined by means of ^{31}P NMR directly from the reaction mixture. Therefore, all further investigations focused on the one-pot cobalt-catalyzed Diels–Alder/Wittig olefination reaction sequence without any isolation of the air-sensitive dihydroaromatic intermediates. The reaction products formed by this reaction sequence were furthermore oxidized by the addition of DDQ to generate the styrene (R = aliphatic) or stilbene (R = aromatic) type products **6** which were then detectable and could be isolated and characterized. Consequently, we report herein a sequential three-step conversion which was performed without the isolation of the dihydroaromatic intermediates of type **4** and **5** in terms of a one-pot process. However, separation of the organic intermediates of type **5** by simple filtration from the cobalt catalyst mixture and its inorganic components was feasible and led to the isolated dihydroaromatic styrene or stilbene intermediates.

The addition of a base and an aldehyde converted the dihydroaromatic and allylic type phosphonium salts **4** into the organic products **5** via the Wittig olefination reaction which could then be detected by GC or GCMS analysis. Therefore, in a series of experiments the reaction time and the cobalt catalyst loading for the cobalt-catalyzed Diels–Alder reactions were optimized using anisaldehyde for the Wittig olefination reaction. The best results were obtained for a protocol in which 10–20 mol % of the catalyst was used in the cobalt-catalyzed Diels–Alder reaction, and the mixture was stirred for 0.5 h at room temperature after which the characteristic color change from green toward a deep brown was observed. Then the base and the aldehyde for the Wittig olefination reaction were added. After further 1–2 h of stirring at ambient temperatures, the dihydroaromatic product **5** could be detected and the conversion estimated by GC and GCMS. The dihydroaromatic products were obtained by simple filtration over a small amount of silica, evaporation of the solvent before further oxidation by DDQ in benzene or toluene to generate the corresponding aromatic products **6**. Without this simple filtration of the dihydroaromatic intermediates from the cobalt–catalyst mixture the yields of the desired products **6** were somewhat diminished if the DDQ oxidation was performed in a straightforward one-pot reaction. The results of the Diels–Alder–Wittig reaction–DDQ oxidation sequences are summarized in Table 1.

The variation of the base gave rather disappointing results. If sodium hydride, sodium amide, or *n*-butyllithium was used as a base, only traces of the product were formed whereas for

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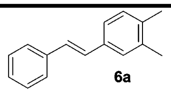
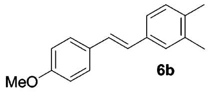
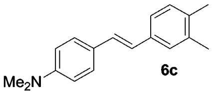
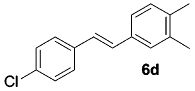
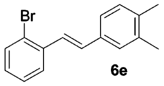
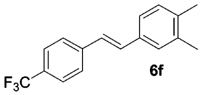
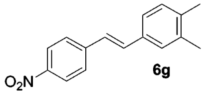
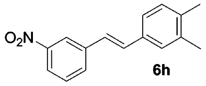
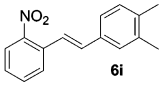
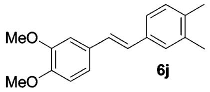
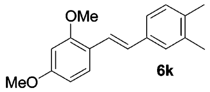
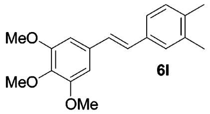
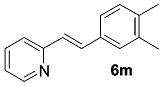
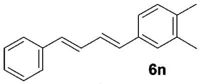
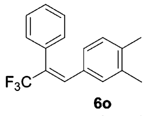
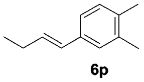
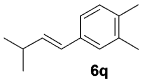
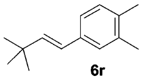
(4) For leading references, see: (a) Hilt, G.; Galbiati, F. *Org. Lett.* **2006**, *8*, 2195. (b) Hilt, G.; Galbiati, F.; Harms, K. *Synthesis* **2006**, 3575. (c) Hilt, G.; Hess, W.; Schmidt, F. *Eur. J. Org. Chem.* **2005**, 2526. (d) Hilt, G.; Lüers, S.; Smolko, K. I. *Org. Lett.* **2005**, *7*, 251. (e) Hilt, G.; Korn, T. J.; Smolko, K. I. *Synlett* **2003**, 241.

(5) (a) Ashburn, B. O.; Carter, R. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 6737. (b) Ashburn, B. O.; Carter, R. G.; Lakharov, L. N. *J. Am. Chem. Soc.* **2007**, *129*, 9109.

(6) In contrast, higher catalyst loadings in the case of sulfur-functionalized alkynes led to the desired conversions. See ref 3f.

TABLE 1. Results for the Cobalt-Catalyzed Diels−Alder/Wittig/DDQ Oxidation Reaction Sequence

Entry	Carbonyl Derivative	Product (6)[a]	Yield (*E* / *Z* Ratio)
1	C_6H_5CHO	 **6a**	94% (1.1 : 1.0)
2	$4\text{-}MeOC_6H_4CHO$	 **6b**	84% (1.7 : 1.0)
3	$4\text{-}Me_2NC_6H_4CHO$	 **6c**	54% *E* only
4	$4\text{-}ClC_6H_4CHO$	 **6d**	57% (1.5 : 1.0)
5	$2\text{-}BrC_6H_4CHO$	 **6e**	66% (1.9 : 1.0)
6	$4\text{-}F_3CC_6H_4CHO$	 **6f**	64% (2.2 : 1.0)
7	$4\text{-}NO_2C_6H_4CHO$	 **6g**	85% (1.5 : 1.0)
8	$3\text{-}NO_2C_6H_4CHO$	 **6h**	82% (2.2 : 1.0)
9	$2\text{-}NO_2C_6H_4CHO$	 **6i**	64% (1.9 : 1.0)
10	$3,4\text{-}(MeO)_2C_6H_3CHO$	 **6j**	63% (1.4 : 1.0)
11	$2,4\text{-}(MeO)_2C_6H_3CHO$	 **6k**	25% (6.7 : 1.0)
12	$3,4,5\text{-}(MeO)_3C_6H_2CHO$	 **6l**	95%[b] (7.0 : 1.0)
13	$2\text{-}CHOC_5H_4N$	 **6m**	69% (1.4 : 1.0)
14	$C_6H_5\text{-}CH{=}CH\text{-}CHO$	 **6n**	64% (1.2 : 1.0)
15	$C_6H_5COCF_3$	 **6o**	58% *E* only
16	CH_3CH_2CHO	 **6p**	22% (40%)[c,d] (1.0 : 1.1)
17	$(H_3C)_2CHCHO$	 **6q**	7% (45%)[c,d] (2.0 : 1.0)
18	$(H_3C)_3CCHO$	 **6r**	44% (1.0 : 2.5)

[a] The compounds **6a**,**b**,**f**,**g**,**j**,**n**,**r** were described previously; see ref 3d. [b] For the optimization process, see the text. [c] Oxidation with TCNE as oxidant. [d] The crude yields of the dihydroaromatic intermediates **5p** and **5q** were 81% and 84%, respectively.

no obvious reason better results were obtained with sodium hexamethyl disilazide (NaHMDS). Nevertheless, all of these bases were inferior to potassium *tert*-butoxide, which was used in all subsequent reactions. The variation of the temperature for the Wittig reaction had no significant effect on the olefination reaction in terms of reactivity or *E*/*Z* stereoselectivity. In general, the conversion of the intermediate **4** with electron-rich as well as electron-poor aromatic aldehydes led to the desired products **6** in acceptable to very good overall yields of up to 95%. The substitution pattern and the nature of the substituents could be varied covering a vast range. In the case of ortho-substituted aldehydes, the steric hindrance by the substituents diminished the yields somewhat (entries 5, 9, and 11). Nevertheless, polyfunctionalized products could be obtained, and particularly interesting were di- and trimethoxylated benzaldehyde derivatives (entries 10−12) which led to products **6j**−**l**, which exhibit some structural similarities to the family of the combretastatine natural products.[7] Also the 1,4-diaryl-substituted 1,3-butadiene **6n** could be obtained in a rather good yield of 64% (entry 14) applying cinnamic aldehyde as starting material. It is noteworthy to point out that for the 4-dimethylamino-functionalized benzaldehyde the *E*-isomer was isolated exclusively. In all other cases, mixtures of the newly formed double bond geometry were observed with a moderate to good preference for the *E*-double bond geometry. The nature of the carbonyl derivative, on the other hand, could not be varied indefinitely, and the range was limited toward aromatic aldehydes and a trifluoromethyl-substituted ketone (entry 15) which could be applied in the reaction sequence with reasonable success. The application of other ketones such as acetone, acetophenone and cyclohexanone gave the desired styrene type products in lower yields (25% for acetophenone, otherwise <5% yield), indicating that the semistabilized phosphonium ylide intermediate is not highly reactive. Nevertheless, for the trifluoromethyl-functionalized ketone (entry 15) only the *E*-isomer was detected. The transformation with the sterically unhindered aliphatic aldehyde such as propanal (entry 16) gave good results of up to 81% for the crude dihydroaromatic derivative of type **5**. Unexpectedly, the following DDQ oxidation of this material led to decomposition and/or polymerization side reactions so that the yield of the desired aromatic product **6p** in this case was considerably diminished. The same behavior was observed for the other aliphatic aldehyde with an allylic proton (entry 17), while the *tert*-butyl-functionalized material **6r** gave a reasonable yield of 44% after DDQ oxidation despite the steric hindrance. Alternatively, the oxidation could be performed with TCNE at ambient temperature in dioxane solution. Under these conditions, the rate of the thermal Diels−Alder reaction of the TCNE with the congested 1,3-diene subunit in the dihydroaromatic derivative as side reaction is only moderate, and the electron-transfer reaction dominates so that the desired aromatic products **6p** and **6q** were obtained in moderate yields of 40% and 45%, respectively.[8] Because the oxidation of the *tert*-butyl-substituted dihydroaromatic intermediate (entry 18) could be performed with DDQ to give the desired product **6r** in 44% yield, a possible

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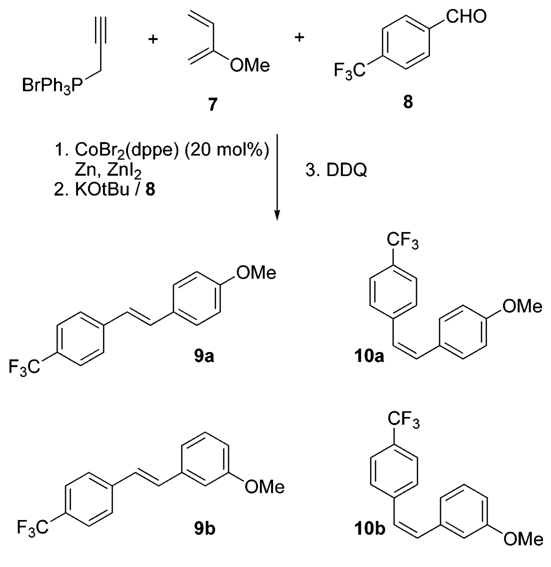
(7) (a) Tron, G. C.; Pirali, T.; Sorba, G.; Pagliai, F.; Busacca, S.; Genazzani, A. A. *J. Med. Chem.* **2006**, *49*, 3033. (b) Cirla, A.; Mann, J. *Nat. Prod. Rep.* **2003**, *20*, 558. (c) Pettit, G. R.; Singh, S. B.; Niven, M. L. *J. Am. Chem. Soc.* **1988**, *110*, 8539.

(8) Ramnial, T.; McKenzie, I.; Gorodetsky, B.; Tsang, E. M. W.; Clyburne, J. A. C. *Chem. Commun.* **2004**, 1054. Sterically hindered alkenyl functionalized dihydroaromatic compounds bearing a 1,3-diene subunit led to a fast redox reaction instead of the desired Diels−Alder reaction; see ref 4d.

SCHEME 3



9a : **10a** : **9b** : **10b** = 41 : 39 : 10 : 10, overall yield 63%

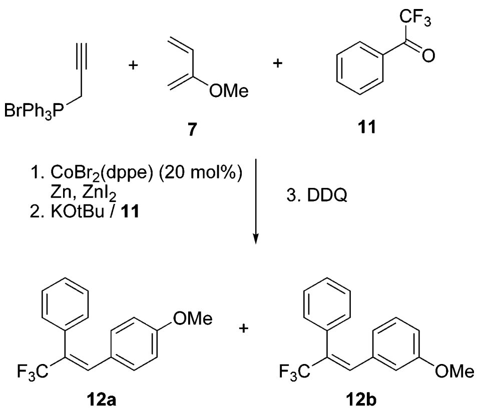
side reaction of the aliphatic-substituted derivatives could be attributed to allylic oxidation processes leading to unidentified side products.

Based on the observation that the *E*/*Z* stereoselectivity of the Wittig olefination of the dihydroaromatic phosphonium salts of type **4** shows in most cases a moderate selectivity for the *E*-configuration of the newly formed double bond of the styrene derivatives, these phosphonium ylides exhibit selectivities located between the stabilized ylides, such as the Wadsworth−Horner−Emmons reagents, and the semistabilized ylides such as the allylic-type phosphonium ylides as was outlined by Berger.[9] As could be shown, the stereoselectivity can be controlled by the nature of the substituents on the phosphorus. Within this study such modifications were not undertaken and remain an option for the generation of enriched *E* or *Z* stereoisomers.[9,10]

The separation of the *E*/*Z* stereoisomers of the products of type **6** by means of column chromatography was accomplished for most derivatives, and pure products could be obtained and characterized. The situation became more complicated when unsymmetrical 1,3-dienes, such as 2-methoxy-1,3-butadiene (**7**), were used as starting materials in the cobalt-catalyzed Diels−Alder reaction. In these cases, not only *E*/*Z* stereoisomers of the newly formed olefinic double bond, as in the products of type **9** and **10**, were encountered but in addition regioisomers (**a** and **b**) generated by the Diels−Alder reaction could be observed (Scheme 3).

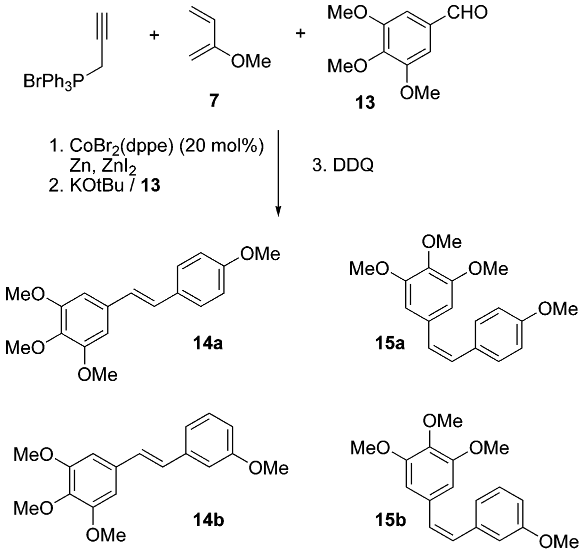
In this case, the separation of the four isomers in pure form could not be achieved by column chromatography. However, from the ^{19}F NMR data of the mixture the ratios of the isomers could be determined while the corresponding GC, ^{1}H NMR, and ^{13}C NMR gave partially overlapping or poorly separated peaks. The situation became easier by the application of trifluoromethyl acetophenone **11** where only the *E*-configured products **12a** and **12b** were observed as could be determined from GC, GCMS, and ^{19}F and ^{13}C NMR data (Scheme 4).

SCHEME 4



12a : **12b** = 88 : 12, overall yield 50%

SCHEME 5



14a : **14b** : **15a** : **15b** = 53:26:16:5, overall yield 63%

On the other hand, if 3,4,5-trimethoxybenzaldehyde **13** was used in the reaction sequence the analysis of the product mixture became more difficult because of the inherent impossibility of a simple analysis by ^{19}F NMR. In addition, as was found in many other cases, the olefinic protons overlap with the aromatic protons but fortunately the methoxy groups of all the four isomers (**14a**,**b** and **15a**,**b**) could be separated in an ^{1}H NMR spectrum (600 MHz) (Scheme 5). As expected, the Wittig olefination also favors the *E*-stereochemistry of the olefinic double bond, while the cobalt-catalyzed Diels−Alder reaction gave predominantly the para-substituted products in moderate selectivity.

Terminal alkynylphosphonium salts are not the only reagents which can be used in the reaction sequence. As could be shown by the application of starting material **16** which bears a phosphonium salt with an internal alkyne functionality, the cobalt-catalyzed Diels−Alder reaction with 2,3-dimethyl-1,3-butadiene led to a dihydroaromatic tetrasubstituted phosphonium

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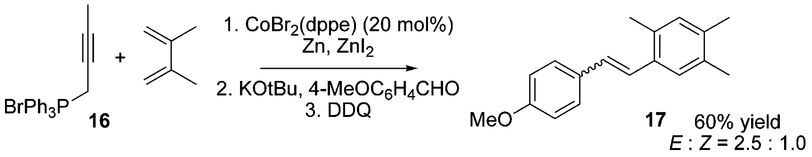
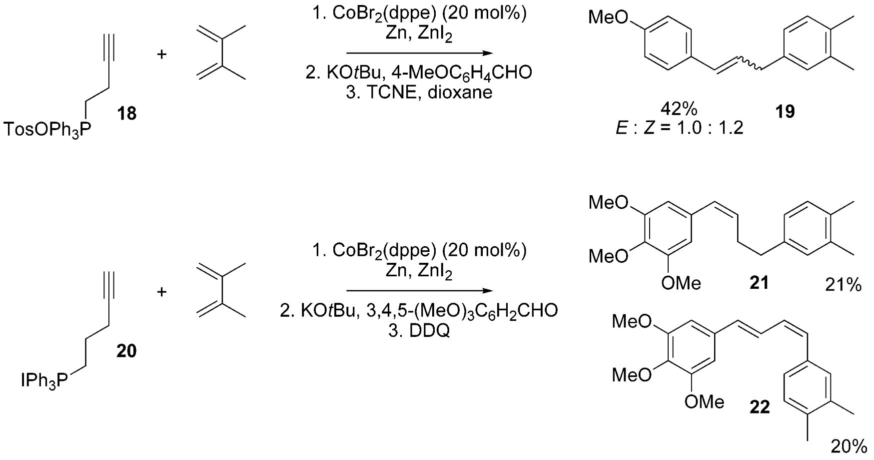
(9) (a) Ackermann, M.; Berger, S. *Tetrahedron* **2005**, *61*, 6764. (b) Appel, M.; Blaurock, S.; Berger, S. *Eur. J. Org. Chem.* **2002**, 1143. (c) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (d) Tamura, R.; Saegusa, K.; Kakihana, M.; Oda, D. *J. Org. Chem.* **1988**, *53*, 2723. (e) Vedejs, E.; Marth, C. F.; Ruggeri, R. *J. Am. Chem. Soc.* **1988**, *110*, 3940. (f) Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1988**, *110*, 3948. (g) Robiette, R.; Richardson, J.; Aggarwal, V. K.; Harvey, J. N. *J. Am. Chem. Soc.* **2006**, *128*, 2394.

(10) (a) Valentine, D. H.; Hillhouse, J. H. *Synthesis* **2003**, 317. (b) Celatka, C. A.; Liu, P.; Panek, J. S. *Tetrahedron Lett.* **1997**, *38*, 5449.

SCHEME 6



SCHEME 7



salt intermediate which was then successfully applied in the Wittig olefination for the synthesis of the styrene product **17** (Scheme 6).

Therefore, higher substituted and more complicated products will be accessible applying phosphonium salts with internal alkynyl functionalities.

In a last set of experiments, longer chained alkynylphosphonium salts such as **18** and **20** were tested (Scheme 7). While the cobalt-catalyzed Diels–Alder reaction and the Wittig olefination could be performed in the same manner as before, again problems were encountered in the DDQ oxidation step. The DDQ oxidation to give the diarylpropene derivative **19** led to decreased yields by oxidative side reactions of the allylic position and formation of unidentified side products.[11] For the longer alkyl chain as shown in **20**, the DDQ oxidation led to side products which could be isolated and characterized. In this case, the DDQ oxidation led not only to the oxidation of the dihydroaromatic substituent to yield product **21** but also to the partial introduction of another double bond to generate product **22**. It is notable that the DDQ oxidation seems to be stereoselective since the *Z*-configured olefin **21** could be isolated in pure form while the *E*-isomer was oxidized by DDQ to yield the diene **22**. In addition, the newly formed double bond in **22** is also formed with good stereoselectivity and the NMR data indicate that **22** consists mainly (>95%) of the 1*E*,3*Z* stereoisomer.

The presented protocol provides a very variable three component access toward unsymmetrically polysubstituted stilbene derivatives from simple and commercially available starting materials. On the other hand, difficulties were encountered as the application of aliphatic aldehydes gave only relatively poor results for propionic aldehyde and pivalyl aldehyde (entries 20, 21).

Summary

The cobalt catalyst system [$CoBr_2$(dppe)/ZnI_2/Zn] represents the first catalyst which is able to efficiently convert arylalkynylphosphonium salt dienophiles in a metal-catalyzed Diels–Alder reaction with acyclic 1,3-dienes. The dihydroaromatic intermediates can be converted in a Wittig olefination with aldehydes to styrene- and stilbene-type products in acceptable to very good yields. The newly formed double bond generated by the olefination reaction exhibits predominantly *E*-geometry, indicating that the phosphorus ylide intermediate can be assigned as a semistabilized ylide. The regioselectivity of the cycloaddition is controlled by steric factors to preferentially give the para-substituted products when unsymmetrical starting materials are used. When longer chained alkynylphosphonium salts are applied, higher homologues are generated, and interestingly, in the case of propene derivatives, side reactions during the DDQ oxidation occur. The oxidation of dihydroaromatic butene derivatives leads to a stereoselective oxidation by DDQ where the *E*-double bond is oxidized to the 1*E*,3*Z*-isomer leaving the *Z*-butene derivative untouched.

Experimental Section

General Methods. All reactions were carried out under an argon atmosphere in flame-dried glassware. Dichloromethane was distilled under nitrogen from P_4O_{10}, and ZnI_2 was dried in vacuo at 150 °C prior to use. Commercially available materials were used without further purification.

Starting Materials. 2-Methoxy-1,3-butadiene[12] as well as the Wittig precursors[13] were prepared according to adapted literature procedures.

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[11] The reaction of 1,3-diphenylpropene with DDQ under otherwise identical reaction conditions did not lead to any considerable transformation of the starting material. Therefore, this behavior seems to be very limited to the DDQ oxidation of the dihydroaromatic propene derivative. Further investigations concerning this new type of reactivity are underway.

[12] Marshall, K. S.; Dolby, L. J. *Org. Prep. Proc.* **1969**, *1*, 229.

[13] (a) Preparation of **3**: Eiter, K.; Oedinger, H. *Liebigs Ann. Chem.* **1965**, *682*, 62. (b) Preparation of **16**: Hann, M. M.; Sammes, P. G.; Kennewell, P. D.; Taylor, J. B. *J. Chem. Soc., Perkin Trans. 1* **1982**, 307. (c) Preparation of **18**: Hanko, R.; Hammond, M. D.; Fruchtmann, R.; Pfitzner, J.; Place, G. A. *J. Med. Chem.* **1990**, *33*, 1163. (d) Preparation of **20**: Sato, K.; Inoue, S.; Ota, S. *J. Org. Chem.* **1970**, *35*, 565.

Representative Procedure for the Diels−Alder/Wittig Olefination Reaction Sequence. Synthesis of (*E*/*Z*)-5-(3,4-Dimethylstyryl)-1,2,3-trimethoxybenzene (6l). Under an argon atmosphere, ZnI_2 (319 mg, 1.0 mmol), zinc dust (39 mg, 0.6 mmol), and $CoBr_2$(dppe) (62 mg, 0.1 mmol) were suspended in anhydrous CH_2Cl_2 (5 mL). After formation of the active catalytic species, recognizable when the color of the suspension turned from green to deep brown, triphenyl(prop-2-ynyl)phosphonium bromide (191 mg, 0.5 mmol) and 2,3-dimethyl-1,3-butadiene (62 mg, 0.75 mmol) were added at room temperature. The resulting mixture was stirred at rt for 30 min. After the solution was cooled with an ice bath, KO-*t*-Bu (280 mg, 2.5 mmol) and 3,4,5-trimethoxybenzaldehyde (147 mg, 0.75 mmol) were added at 0 °C. After additional stirring at room temperature for 1 h, the solids were removed by filtration over a short pad of silica gel (eluent: pentane/MTBE = 1:1). After the solvent was evaporated, the crude product was dissolved in benzene (10 mL) and DDQ (136 mg, 0.6 mmol) was added. After the resulting mixture was stirred at room temperature for 1 h, it was washed twice with basic thiosulfate solution (10% NaOH/10% $Na_2S_2O_3$, 10 mL). The aqueous phases were combined and extracted with MTBE (20 mL), and the combined organic phases were dried ($MgSO_4$). After the solvent was evaporated under reduced pressure, the crude product was purified by column chromatography (eluent: pentane/ethyl acetate = 10:1). The product was obtained as a white solid (141 mg, 95%).

E-isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.33 (s, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.01 (s, 2H), 6.76 (s, 2H), 3.94 (s, 6H), 3.90 (s, 3H), 2.31 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.0, 136.3, 135.7, 134.9, 132.9, 130.2, 130.2, 129.6, 129.4, 126.4, 113.6, 106.3, 61.0, 56.0, 19.7, 19.6.

Z-isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.09 (s, 1H), 7.05 (d, *J* = 7.9 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.53 (d, *J* = 12.1 Hz, 1H), 6.52 (s, 2H), 6.43 (d, *J* = 12.2 Hz, 1H), 3.84 (s, 3H), 3.67 (s, 6H), 2.22 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.5, 137.9, 136.8, 136.3, 134.9, 133.5, 130.1, 128.3, 127.8, 127.5, 124.0, 103.6, 61.0, 56.2, 19.9, 19.6; MS (EI) *m*/*z* = 298 (M^+), 283, 223, 208, 195, 180, 165, 153, 133; HRMS *m*/*z* calcd for $C_{19}H_{22}O_3$ 298.1569, found 298.1564; IR (KBr) 2917, 1582, 1506, 1449, 1420, 1339, 1260, 1239, 1127, 1009, 959, 852, 818, 631.

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Supporting Information Available: Characterization data for compounds **6a**−**r**, **9a**,**b**, **10a**,**b**, **12a**,**b**, **14a**,**b**, **15a**,**b**, **17**, **19**, and **21**−**22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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