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CCl_4-TMEDA-CuCl—A Novel Convenient Catalytic System for Dimerization of Terminal Acetylenes in Mild Conditions

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Abstract: A novel catalytic system for homocoupling terminal acetylenes was elaborated based on CuCl as a catalyst (10 mol%), TMEDA as a base and CCl_4 as an oxidant. The influence of the solvent, base, amount of catalyst and CCl_4 on the reaction was investigated. Methanol was found to be the solvent of choice. The broad synthetic scope of the reaction was demonstrated. Diynes with various substituents were prepared in up to 92% yields. The possible reaction mechanism is discussed.

Keywords: tetrachloromethane; acetylene; oxidative homocoupling; diyne; copper

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1. Introduction

Several years ago, a novel catalytic olefination reaction of carbonyl compounds (COR) was discovered in our laboratory [1,2]. It was found that *N*-unsubstituted hydrazones of carbonyl compounds transform into alkenes under treatment of polyhaloalkanes (PHA) in the presence of a base (ammonia, ethylenediamine, triethylamine) and catalytic amounts of copper salts. The reaction is accompanied by the evolution of nitrogen, and azines are formed as the only by-products (Scheme 1). The reaction has a broad synthetic scope and allows the synthesis of alkenes containing various halogens and functional groups in yields of up to 90–95% [3–6]. It is worth noting the high stereoselectivity of the reaction; in some cases, the ratio of diastereoisomers reaches 21:1 [7] (Figure 1). The use of freons as olefinating reagents allows the synthesis of fluorine-containing alkenes, convenient building blocks for the synthesis of more complex fluorinated compounds with important practical applications [8–12].

It was found that the PHA-nitrogen base-copper salt system also works for the transformation of a number of other types of hydrazones. In particular, the application of this system made it possible to oxidize isatin hydrazones to the corresponding diazoketones [13]. It was also found that N-substituted hydrazones can be converted into the corresponding halogenated azabutadienes [14] (Figure 1).

Conjugated diynes are under intensive investigations due to their unique properties [15–18]. They are valuable materials for various synthetic transformations [19,20]. In particular, they have found application in the preparation of natural products [21,22], pharmaceuticals [23], π-conjugated acetylene polymers [24,25], modern construction materials [26,27], heterocyclic compounds [28], electronic and optical materials [29,30]. Conjugated 1,3-diynes also possess biological activity [21], showing antifungal [31], antibacterial [32], anti-inflammatory [33], anti-HIV [34] and anticancer properties [35].

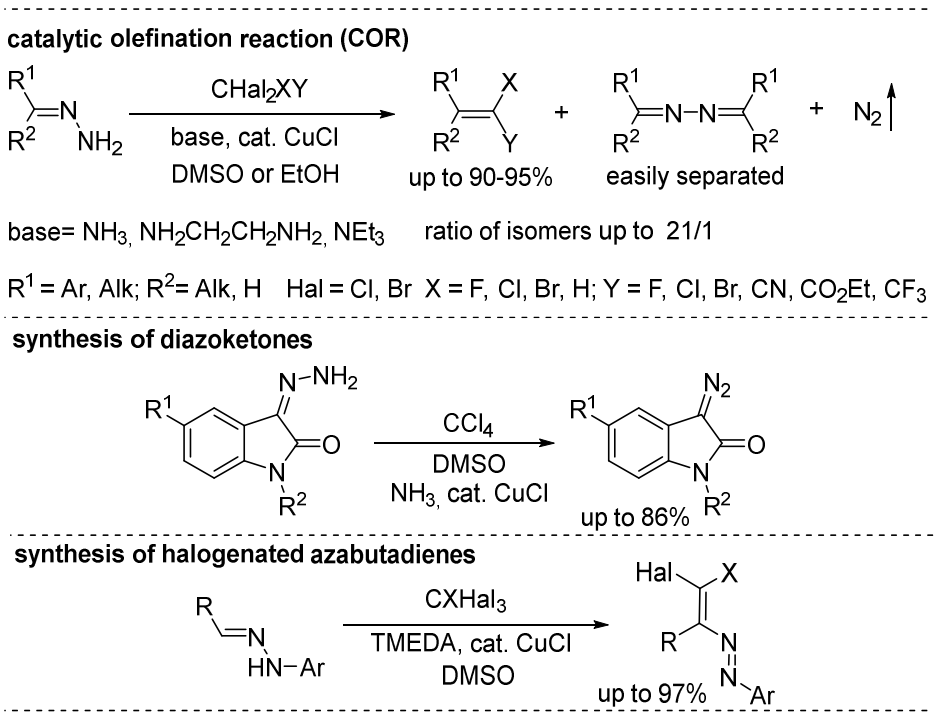
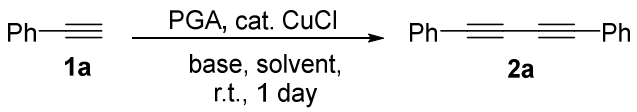


Figure 1. The use of the PHA-nitrogen base-CuCl system in the organic synthesis.



Solvent	quantity of CuCl	Base	quantity of CCl_4	PGA
2.5 equiv. CCl_4, 0.1 equiv. CuCl 2.2 equiv. TMEDA	2.5 equiv. CCl_4, 2.2 equiv. TMEDA MeOH	2.5 equiv. CCl_4 0.1 equiv. CuCl MeOH	2.2 equiv. TMEDA 0.1 equiv. CuCl MeOH	0.1 equiv. CuCl 2.2 equiv. TMEDA MeOH
Solvent (**2a**)	CuCl, mol% (**2a**)	2.2 equiv. Base (**2a**)	CCl_4, equiv. (**2a**)	2.5 equiv. PGA (**2a**)
MeCN (63%)	20 (74%)	en (traces%)	1 (76%)	$CFBr_3$ (86%)
DMSO (48%)	**10 (92%)**	NEt_3 (traces%)	1.5 (82%)	$CF3CCl_3$ (78%)
THF (23%)	5 (85%)	NH_3 (4%)	**2.5 (92%)**	$CBrCl_3$ (93%)
EG (63%)	2 (62%)	**TMEDA (92%)**	5 (92%)	CBr_4 (94%)
i-PrOH (72%)	1 (51%)			**CCl_4 (92%)**
EtOH (90%)	0 (0%)			
MeOH (92%)				

Scheme 1. Screening of the conditions for the dimerization of phenylacetylene.

The most efficient method for the synthesis of conjugated diynes is the oxidative dimerization of terminal acetylenes, which is known as the Glaser reaction [15,36–38]. The original Glaser reaction used equivalent amounts of copper salts, ammonia (Glaiser[39]) or pyridine (Eglinton [40,41]) as the bases. Later, catalytic variants using various copper salts and ligands were also successfully developed. In particular, Hay proposed the O_2-TMEDA-CuCl system, which allows dimerization of terminal acetylenes using catalytic amounts of copper salts [42,43]. This catalytic system has become a very popular system for the dimerization of terminal alkynes [44]. Nevertheless, the search for novel conditions for the Glaser reaction is still an ongoing process. For example, a cooperative behavior of nickel [45–48], iron [49] and palladium [50–53] based catalysts has been reported for copper-catalyzed alkyne coupling. Heterogeneous catalysis has also been used for this

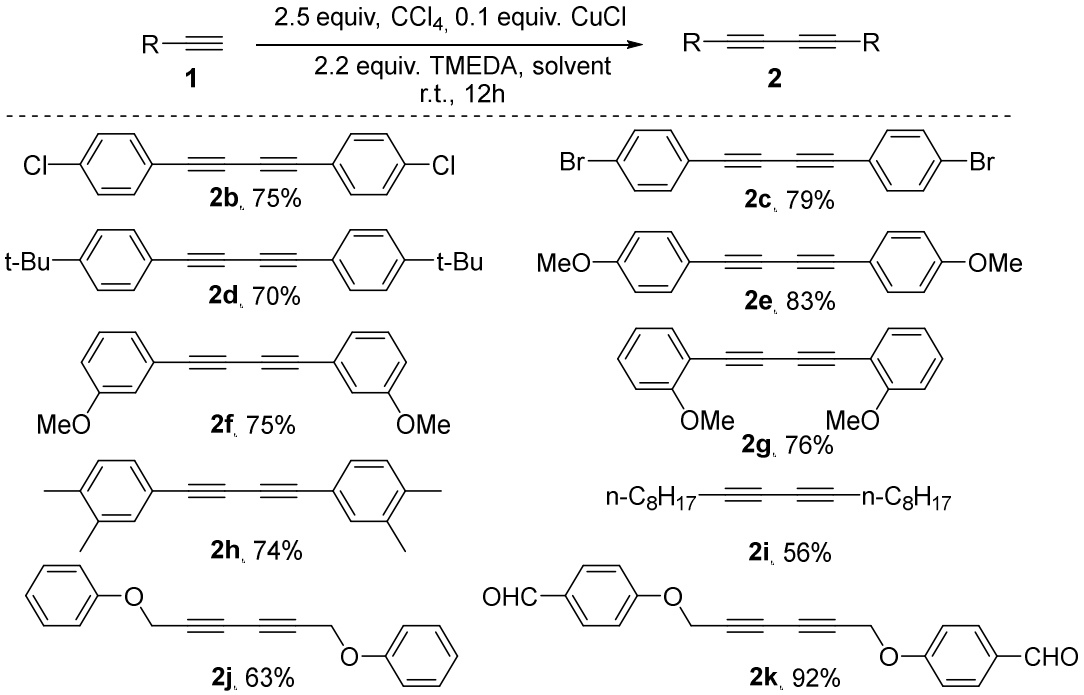
aim. For example, copper hydroxide on TiO_2 [54], cuprous chloride-doped zeolites [55–57], silica-supported Cu(II)-hydrazone coordination compounds [58], $Cu_3(BTC)_2$ metal organic framework [59] and even naturally occurring copper-containing minerals, chalcocite (Cu_2S) and bornite (Cu_5FeS_4) [60], have demonstrated high efficiency as catalysts for terminal alkyne coupling. The reaction was also performed in supercritical fluids [61,62], water [63,64], ionic liquids [65,66] and solvent-free conditions [67,68] and under photocatalysis [69]. However, no other oxidants instead of O_2 were found in the literature. In our opinion, the use of other oxidants and performing the reaction in homogeneous conditions could be very attractive. It should be noted that oxidant-TMEDA-Cu systems are of great interest for the modern methodology of oxidations. Thus, these systems were employed for the synthesis of hydrazine compounds from secondary anilines via the oxidative formation of a N−N bond [70] and for the oxidation of primary alcohols into aldehydes [71,72]. This study is devoted to the investigation of the dimerization of terminal acetylenes using the CCl_4-TMEDA-CuCl system.

2. Results

The study of the reaction mechanism of the catalytic olefination reaction showed that the reaction starts with the oxidation of copper (I) chloride with a polyhaloalkane in the presence of a nitrogen-containing ligand to form a complex of copper (II) chloride and a polyhalogenated alkyl radical. The regeneration of copper (I) proceeds under the action of either hydrazone or the addition of products of polyhaloalkyl radicals to hydrazone [73]. Thus, the PHA-nitrogen base-CuCl system works as an oxidizing agent. As a part of the further study of the synthetic possibilities of this system, we decided to study it for the dimerization of terminal acetylenes. TMEDA was chosen as a base and carbon tetrachloride as an oxidant. First, we investigated the influence of the nature of the solvent on the course of the reaction. The reaction was carried out at room temperature using 10 mol% of CuCl. We found that under the action of the CCl_4-TMEDA-CuCl system, the model substrate (phenylacetylene) was successfully dimerized to 1,3-diyne **2a** (Scheme 1). The reaction proceeds both in polar aprotic solvents and in alcohols. The best reaction yields (90–92%) were achieved in ethanol and methanol. In contrast, the yields in coordinating solvents (MeCN, THF and DMSO) did not exceed 63% due to possible poisoning of the catalytic system. Next, we studied an effect of the amount of catalyst on the reaction outcome. It turned out that the reaction proceeds even with 1 mol% of CuCl; however, in this case, the conversion time of phenylacetylene increases to about 2 days, and the yield of target 1,3-diyne **2a** decreases to 51%. The use of a 10 mol% catalyst turned out to be optimal, since in this case the highest yield of 1,3-diyne **2a** was observed. It should be noted that the reaction does not take place without CuCl (Scheme 1). We also tested several other nitrogen-containing bases in the reaction. In the case of ethylenediamine, triethylamine and ammonia, the yield dropped to 4% due to massive tarring of the reaction mixture. It was reported that TMEDA (which is the bidentate tertiary amine ligand) provides enhanced solubility to the reactive copper intermediate [44]. We believe that it is a reason for such a dramatic difference in efficiency between TMEDA and other investigated nitrogen-containing bases. Indeed, TMEDA works effectively as both a base and a ligand for the coordination with copper.

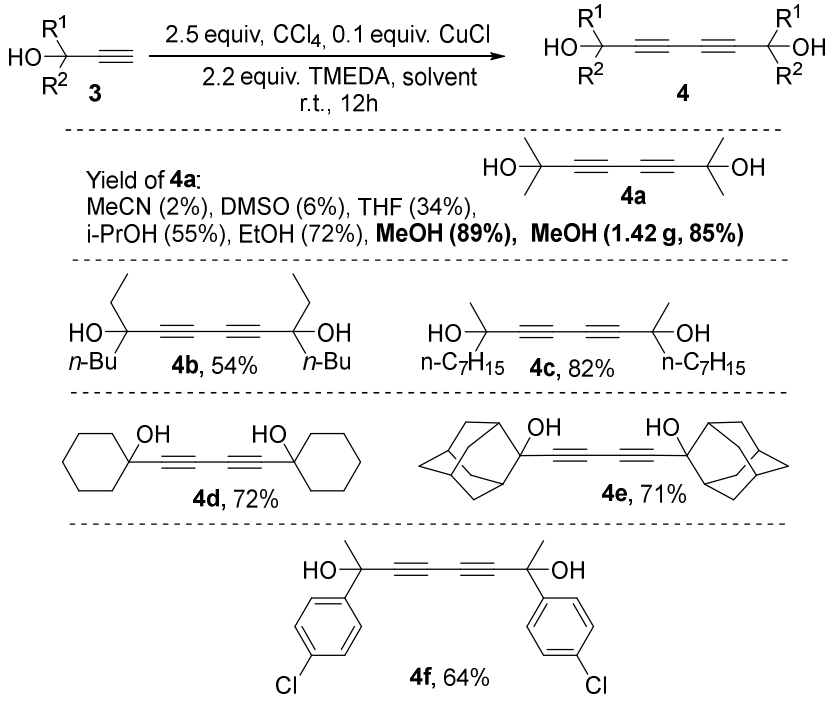
Next, we performed a series of experiments using various amounts of CCl_4. We found that the reaction proceeds in high yield (76%) even with one equivalent of CCl_4. The yield of diyne **2a** increases until the amount of PHA increases to 2–2.5 equiv., after which it remains constant. As a proof of principle, we tested several other PHAs. It was found that $CFBr_3$, CF_3CCl_3, $CBrCl_3$ and CBr_4 are also suitable for the dimerization of alkynes to afford diyne **2a** in 78–94% yields. However, using CCl_4 is preferable because of its very affordable price. Concluding this part of the investigation, we found that the optimal condition for the reaction is to perform it in methanol with TMEDA as a base, using 2.5 equivalents of carbon tetrachloride and 10 mol% of CuCl.

Having found the optimal conditions for the dimerization of phenylacetylene, we carried out a series of reactions with a number of other terminal arylacetylenes. We found that the reaction proceeds in high yield for acetylenes bearing both acceptor and donor substituents at the aromatic ring (Scheme 2). Sterically hindered 2-methoxyphenylacetylene was also successfully involved in the reaction. The corresponding 1,3-diyne **2g** was obtained in a 76% yield. We found that this catalytic system also works well for the dimerization of alkylacetylenes. Thus, 1,3-diyne **2i** was obtained in a good yield from dec-1-yne. Phenylpropargyl ethers were also successfully involved in the reaction to give the corresponding 1,3-diynes **2j**,**2k** in a high yield (Scheme 2). It should be noted that the reaction is tolerated by a carbonyl function. Thus, 1,3-diyne **2k** containing carbonyl groups was isolated in a 92% yield.



Scheme 2. The reaction scope.

To further study the synthetic potential of the reaction, we investigated the dimerization of substituted propargyl alcohols under the action of the CCl_4-TMEDA-CuCl system. We found that, in contrast to aryl- and alkylacetylenes, the solvent affects the reaction much more significantly. Thus, in polar aprotic solvents, the dimerization reaction of propargyl alcohol **3a** proceeds in low yields, not exceeding 4–6%. On the contrary, in alcohols, the reaction proceeds in good to high yields, and methanol also resulted as the optimal solvent for dimerization, in which diyne **4a** was obtained in an 89% yield (Scheme 3). More complex propargyl alcohols have also been successfully involved in the dimerization. Diynes bearing long alkyl chains (**4b**,**4c**), derivatives containing cyclic fragments (**4d**,**4e**) and aryl substituents (**4f**) were obtained efficiently. It should be noted that we synthesized diyne **4a** in gram scale amounts (1.42 g), while the yield remained the same (85%). However, our attempts to carry out dimerization of parent propargyl alcohol were not successful due to massive tarring of the reaction.



Scheme 3. The dimerization of propargyl alcohol derivatives.

The diacetylene diols obtained are interesting compounds from the point of view of medicinal chemistry. Compounds with a moiety of conjugated polyacetylene alcohols have been isolated from various natural sources. Thus, many polyacetylene derivatives have been isolated from *Oplopanax horridus* and *Panax ginseng* plants belonging to the *Araliaceae* family, which exhibit antitumor, anti-inflammatory, antibacterial, antiviral, antifungal, immunomodulatory, neuroprotective, antidressing, hypoglycemic, hepatoprotective activity, as well as activity associated with obesity control (Figure 2) [74]. Recently, three new polyacetylene alcohols extracted from the sea sponge *Siphonochalina Siphonella* in Egypt were found to have activity against a human cervical cancer cell line (HeLa), a human breast cancer cell line (MCF-7) and a human lung cancer cell line. (A549) [75,76].

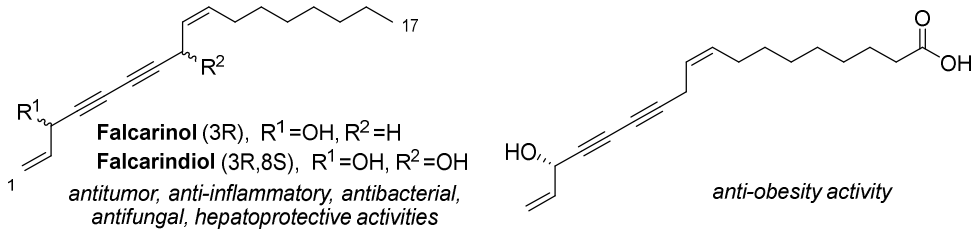
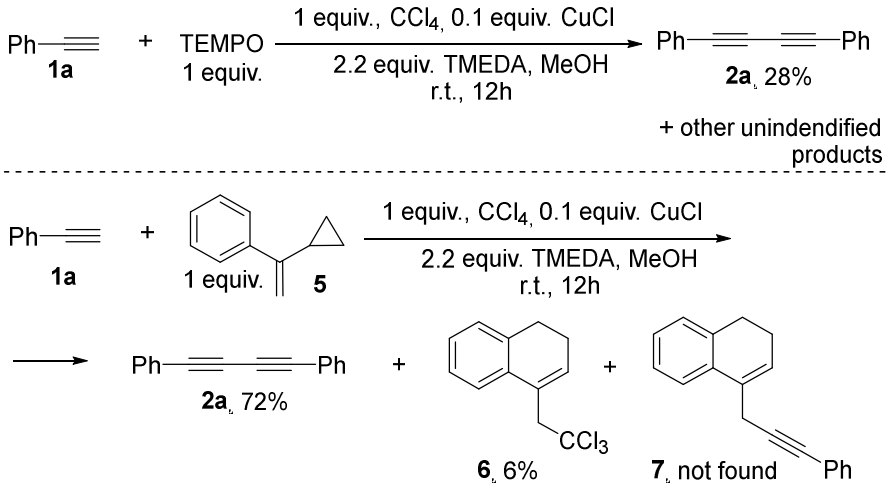


Figure 2. Selected examples of physiologically active diacetylene diols.

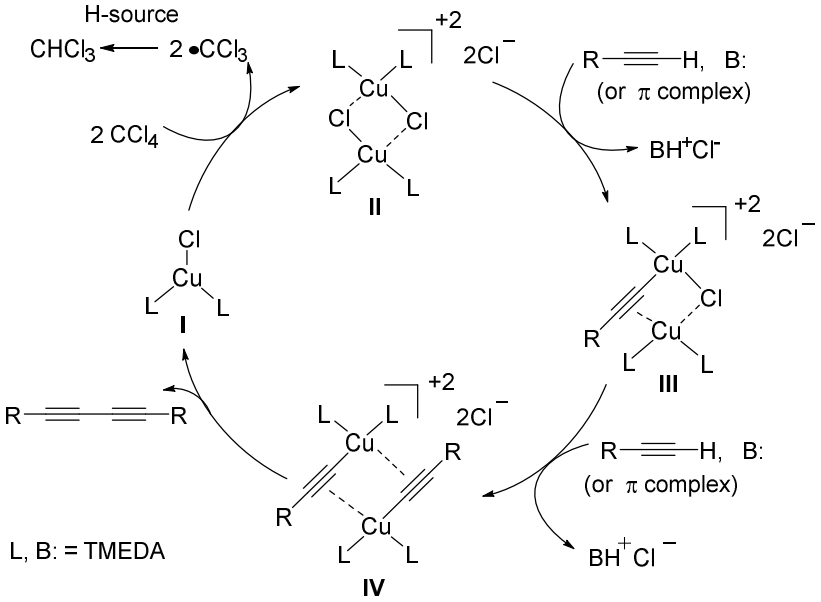
Eventually, we focused our attention on the possible reaction mechanism. It has previously been found that single electron transfer (SET) from CuCl to CCl_4 generates Cu(II) species and the CCl_3 radical [14]. In order to check this possibility for the dimerization of acetylenes, we performed the reaction in the presence of one equivalent of TEMPO, which is a very effective radial scavenger. We found that TEMPO does not completely block the consumption of phenylacetylene and the formation of diyne **2a**. However, noticeable tarring of the reaction was observed to give diyne **2a** in a lower yield compared to the reaction without TEMPO. Next, we carried out the reaction in the presence of one equivalent of α-cyclopropylstyrene. It was found that diyne **2a** is formed in a slightly lower yield

(72% compared to 92%). At the same time, dehydronaphthalene **6** was found in the reaction mixture by ^{1}H NMR. However, no formation of compound **7** was detected. This product could be formed by the addition of phenylacetylenyl radical to α-cyclopropylstyrene. Therefore, the reaction proceeds through the participation of trichloromethyl radical (Scheme 4).



Scheme 4. Control experiments.

Taking into account these results and the literature data about the Glaser reaction mechanism, the following scheme of the reaction can be proposed (Scheme 5) [36,44,77]. Oxidation of the Cu(I) complex I under the action of CCl_4 starts the catalytic cycle to form Cu(II) II complex. Next, complex II reacts with alkyne (or the copper π-complex of alkyne) in the presence of a base (TMEDA) to give intermediate III. The subsequent reaction of III with another molecule of alkyne (or alkyne π-complex) results in the formation of copper complex IV, which is a key reaction intermediate. The reductive elimination of copper from IV provides the target bis-alkyne and Cu(I) complex I to restart the catalytic cycle.



Scheme 5. Possible reaction mechanism.

In conclusion, we developed a new catalytic system (CCl_4-TMEDA-CuCl) for the oxidative dimerization of terminal acetylenes. It was found that terminal acetylenes can be dimerized in yields up to 92% under the action of carbon tetrachloride in methanol in the presence of TMEDA and catalytic amounts of CuCl. The reaction has a wide synthetic scope, allowing the synthesis of conjugated diynes containing both aromatic substituents and aliphatic substituents. Terminal acetylenes containing functional groups were also successfully involved in the reaction to convert into conjugated diynes in up to 92% yield.

3. Materials and Methods

General remarks. ^1H, and ^{13}C NMR spectra (Supplementary Materials) were recorded on a Bruker AVANCE 400 MHz spectrometer in acetone-d_6 and $CDCl_3$ at 400.1 and 100.6 MHz, respectively. Chemical shifts (δ) in ppm are reported with the use of the residual CD_3COCHD_2 and chloroform signals (2.04, 7.25 for ^1H and 29.80, 77.0 for ^{13}C) as internal reference. The coupling constants (J) are given in Hertz (Hz). HRMS spectra were measured using the MicroTof Bruker Daltonics instrument. A TLC analysis was performed on "Macherey-Nagel ALUGRAM Xtra SIL G/UV_{254}" plates. Column chromatography was performed on silica gel "Macherey-Nagel 0.063–0.2 nm (Silica 60)". All reagents were of reagent grade and were used as such or were distilled prior to use. Terminal acetylenes were prepared by literature procedures (**1b**,**c**,**d**,**e**,**h** [78]; **3b**,**c**,**d**,**e**,**f** [79]) or purchased from commercial suppliers (**1a**,**f**,**g**,**i**,**j**,**k**; **3a**). Melting points were determined on Electrothermal 9100 apparatus. Due to the reported toxicity [80] of CCl_4, all manipulations with this reagent should be carried out with care.

Screening of the optimal conditions for the dimerization of phenylacetylene (general procedures). *Screening of the optimal solvent*. An 8 mL vial with a screw cap was charged with phenylacetylene **1a** (1 mmol), the corresponding solvent (3 mL), TMEDA (0.32 mL, 2.2 mmol), CCl_4 (0.25 mL, 2.5 mmol) and CuCl (10 mg, 0.1 mmol were added at stirring by a magnetic stirrer). The reaction mixture was stirred for 1 day at room temperature and then broken by 0.1 M of HCl (30 mL). The product was extracted by CH_2Cl_2 (3 × 10 mL); the organic phase was washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated in vacuo; the residue formed was purified by column chromatography on silica gel using gradient elution by hexane, followed by a hexane-CH_2Cl_2 mixture (3:1).

Screening of the optimal amount of CuCl. The procedure for screening the optimal solvent was used with the only difference that the reaction was carried out in methanol and the appropriate amount of CuCl was used instead of 0.1 mmol (10% mmol) of CuCl.

Screening of the optimal base. The procedure for screening of the optimal solvent was used with the only difference that the reaction was carried out in methanol and the corresponding base was used instead of TMEDA.

Screening of the optimal amount of CCl_4. The procedure for screening of the optimal solvent was used with the only difference that the reaction was carried out in methanol and the appropriate amount of CCl_4 was used instead of 0.25 mL (2.5 mmol) of CCl_4.

Screening of the optimal base. The procedure for screening of the optimal solvent was used with the only difference that the reaction was carried out in methanol and the corresponding PHA was used instead of CCl_4.

Dimerization of terminal acetylenes 1 (general procedure). An 8 mL vial with a screw cap was charged with corresponding acetylene **1** (1 mmol), MeOH (3 mL), TMEDA (0.32 mL, 2.2 mmol), CCl_4 (0.25 mL, 2.5 mmol) and CuCl (10 mg, 0.1 mmol were added at stirring by a magnetic stirrer). The reaction mixture was stirred for 1 day and then broken by 0.1 M of HCl (30 mL). The product was extracted by CH_2Cl_2 (3 × 10 mL); the organic phase was washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated in vacuo; the residue formed was purified by passing through a short silica gel pad of silica gel using gradient eluation by hexane, followed by a hexane-CH_2Cl_2 mixture (3:1) for **2a-2j**; and by a hexane-CH_2Cl_2 mixture (3:1) followed by CH_2Cl_2 for **2k**.

1,4-Diphenylbuta-1,3-diyne (2a). Obtained from phenylacetylene **1a** (102 mg, 1 mmol). Pale yellow solid, m.p. 86–88 °C, (Lit. [81] 86–88 °C), R_F 0.55 (hexane-CH_2Cl_2, 3:1), yield 93 mg (92%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.32–7.43 (m, 3H), 7.55–7.58 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 73.9, 81.5, 121.7, 128.4, 129.2, 132.4. NMR data are in agreement with those in the literature [82].

1,4-Bis(4-chlorophenyl)buta-1,3-diyne (2b). Obtained from 1-chloro-4-ethynylbenzene **1b** (143 mg, 1.048 mmol). White powder, m.p. 259–262 °C, (Lit. [83] 258–259 °C), R_F 0.63 (hexane-CH_2Cl_2, 3:1), yield 106 mg (75%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.31 (d, 2H, *J* = 8.4), 7.44 (d, 2H, *J* = 8.4). NMR data are in agreement with those in the literature [82].

1,4-Bis(4-bromophenyl)buta-1,3-diyne (2c). Obtained from 1-bromo-4-ethynylbenzene **1c** (181 mg, 1 mmol). Pale beige powder, m.p. 262–264 °C, (Lit. [84] 260.1–262.3 °C), R_F 0.68 (hexane-CH_2Cl_2, 3:1), yield 143 mg (79%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.37 (d, 2H, *J* = 8.6), 7.47 (d, 2H, *J* = 8.6). NMR data are in agreement with those in the literature [85].

1,4-Bis(4-(tert-butyl)phenyl)buta-1,3-diyne (2d). Obtained from 1-(*tert*-butyl)-4-ethynylbenzene **1d** (149 mg, 0.943 mmol). Pale beige powder, m.p. 208–211 °C, (Lit. [84] 209–210 °C), R_F 0.8 (hexane-CH_2Cl_2, 3:1), yield 104 mg (70%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 1.33 (s, 9H), 7.37 (d, 2H, *J* = 8.4), 7.48 (d, 2H, *J* = 8.4). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 31.1, 34.9, 73.5, 81.5, 118.8, 125.4, 132.2, 152.5. NMR data are in agreement with those in the literature [84].

1,4-Bis(4-methoxyphenyl)buta-1,3-diyne (2e). Obtained from 1-ethynyl-4-methoxybenzene **1e** (131 mg, 0.992 mmol). Pale yellow powder, m.p. 140–142 °C, (Lit. [84] 137.5–139.2 °C), R_F 0.2 (hexane-CH_2Cl_2, 3:1), yield 108 mg (83%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 3.80 (s, 3H), 6.85 (d, 2H, *J* = 8.9), 7.46 (d, 2H, *J* = 8.9). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 55.3, 72.9, 81.2, 113.8, 114.1, 134.0, 160.2. NMR data are in agreement with those in the literature [84].

1,4-Bis(3-methoxyphenyl)buta-1,3-diyne (2f). Obtained from 1-ethynyl-3-methoxybenzene **1f** (141 mg, 1.068 mmol). White powder, m.p. 92–93 °C, (Lit. [64] 92–93 °C), R_F 0.3 (hexane-CH_2Cl_2, 3:1), yield 105 mg (75%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 3.80 (s, 3H), 6.93 (ddd, 1H, *J* = 8.0, *J* = 2.5, *J* = 1.0), 7.05 (dd, 1H, *J* = 2.5, *J* = 1.4), 7.13 (dt, 1H, *J* = 8.0, *J* = 1.2), 7.46 (t, 1H, *J* = 8.0). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 55.2, 73.6, 81.5, 116.0, 117.0, 122.6, 125.0, 129.5, 159.2. NMR data are in agreement with those in the literature [84].

1,4-Bis(2-methoxyphenyl)buta-1,3-diyne (2g). Obtained from 1-ethynyl-2-methoxybenzene **1g** (132 mg, 1 mmol). White powder, m.p. 137–139 °C, (Lit. [64] 137–138 °C), R_F 0.5 (hexane-CH_2Cl_2, 1:1), yield 100 mg (76%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 3.88 (s, 3H), 6.86–6.92 (m, 2H), 7.13 (td, 1H, *J* = 7.9, *J* = 1.7), 7.47 (dd, 1H, *J* = 7.6, *J* = 1.7). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 55.7, 77.9, 78.6, 110.6, 111.2, 120.4, 130.5, 134.3, 161.3. NMR data are in agreement with those in the literature [84].

1,4-Bis(3,4-dimethylphenyl)buta-1,3-diyne (2h). Obtained from 4-ethynyl-1,2-dimethylbenzene **1h** (130 mg, 1 mmol). White powder, m.p. 164–166 °C, R_F 0.65 (hexane-CH_2Cl_2, 3:1), yield 96 mg (74%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 2.25 (s, 3H), 2.28 (s, 3H), 7.09 (d, 1H, *J* = 7.8), 7.28 (dd, 1H, *J* = 7.7, *J* = 1.4), 7.31 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 19.6, 19.9, 73.2, 81.6, 119.0, 129.7, 129.9, 133.4, 136.8, 138.3. NMR data are in agreement with those in the literature [86].

Icosa-9,11-diyne (2i). Obtained from dec-1-yne **1i** (137 mg, 0.992 mmol). Pale brown oil, yield 76 mg (56%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 0.87 (t, 6H, *J* = 6.8), 1.22–1.36 (m, 20H), 1.46–1.54 (m, 4H), 2.23 (t, 4H, *J* = 7.0). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 14.1, 19.2, 22.6, 28.3, 28.8, 29.05, 29.14, 31.8, 65.2, 77.6. NMR data are in agreement with those in the literature [60].

1,6-Diphenoxyhexa-2,4-diyne (2j). Obtained from (prop-2-yn-1-yloxy)benzene **1i** (135 mg, 1.023 mmol). Pale beige powder, m.p. 78–80 °C, (Lit. [87] 77–79 °C), R_F 0.2 (hexane-CH_2Cl_2, 3:1), yield 84 mg (63%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 4.75 (s, 2H), 6.96–6.99 (m, 2H), 7.02–7.05 (m, 1H), 7.31–7.36 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 56.0,

70.9, 74.6, 114.7, 121.7, 129.5, 157.3. NMR data are in agreement with those in the literature [88].

4,4′-(Hexa-2,4-diyne-1,6-diylbis(oxy))dibenzaldehyde (2k). Obtained from 4-(prop-2-yn-1-yloxy)benzaldehyde **1k** (159 mg, 0.994 mmol). Pale beige powder, m.p. 154–158 °C, yield 145 mg (92%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 4.83 (s, 4H), 7.03 (d, 4H, *J* = 8.8), 7.84 (d, 4H, *J* = 8.8), 9.89 (s, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 56.2, 71.4, 73.9, 115.1, 130.7, 131.9, 162.0, 190.7. NMR data are in agreement with those in the literature [87].

Dimerization of terminal acetylenes 3 (general procedure). An 8 mL vial with a screw cap was charged with corresponding acetylene **3** (1 mmol), MeOH (3 mL), TMEDA (0.32 mL, 2.2 mmol), CCl_4 (0.25 mL, 2.5 mmol) and CuCl (10 mg, 0.1 mmol were added at stirring by a magnetic stirrer). The reaction mixture was stirred for 1 day and then broken by 0.1 M of HCl (30 mL). The product was extracted by CH_2Cl_2 (3 × 10 mL); the organic phase was washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated in vacuo; the residue formed was purified by passing through a short silica gel pad of silica gel using gradient eluation by CH_2Cl_2, followed by CH_2Cl_2-MeOH mixture (30:1).

2,7-Dimethylocta-3,5-diyne-2,7-diol (4a). Obtained from 2-methylbut-3-yn-2-ol **3a** (84 mg, 1 mmol). White powder, m.p. 124–126 °C, yield 74 mg (89%). ^{1}H NMR (acetone-d_6, 400.1 MHz): δ 1.43 (s, 12H, 4CH_3), 4.59 (s, 2H, 2OH). $^{13}C\{^1H\}$ NMR (acetone-d_6, 100.6 MHz): δ 31.4, 65.0, 66.0, 85.5. NMR data are in agreement with those in the literature [45].

5,10-Diethyltetradeca-6,8-diyne-5,10-diol (4b). Obtained from 3-ethylhept-1-yn-3-ol **3b** (143 mg, 1.021 mmol). Yellow-brown oil, yield 77 mg (54%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): 0.91 (t, 6H, 2CH_3, *J* = 7.3), 1.02 (t, 6H, 2CH_3, *J* = 7.3), 1.29–1.38 (m, 4H, 2CH_2), 1.41–1.49 (m, 4H, 2CH_2), 1.57–1.73 (m, 8H, 4CH_2), 2.01 (s, 2H, 2OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 8.5, 14.0, 22.8, 26.3, 34.7, 41.1, 68.4, 72.2, 82.0.

8,13-Dimethylicosa-9,11-diyne-8,13-diol (4c). Obtained from 3-methyldec-1-yn-3-ol **3c** (169 mg, 1.004 mmol). Pale brown oil, yield 138 mg (82%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 0.87 (t, 6H, 2CH_3, *J* = 6.9), 1.21–1.34 (m, 16H, 8CH_2), 1.40–1.52 (m, 10H, 2CH_2, 2CH_3), 1.59–1.71 (m, 4H, 2CH_2), 2.02 (s, 2H, 2OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 14.1, 22.6, 24.6, 29.2, 29.5, 29.6, 31.8, 43.5, 67.4, 68.7, 83.2. HRMS (ESI-TOF): m/z [M-OH]$^+$ Calcd for $C_{22}H_{37}O^+$: 317.2839; found: 317.2848.

1,1′-(Buta-1,3-diyne-1,4-diyl)bis(cyclohexan-1-ol) (4d). Obtained from 1-ethynylcyclohexan-1-ol **3d** (124 mg, 1 mmol). Colorless oil, yield 88 mg (72%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 1.15–1.30 (m, 2H, CH_2), 1.44–1.75 (m, 14H, 7CH_2), 1.83–1.95 (m, 4H, 2CH_2), 2.23 (s, 2H, 2OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 23.1, 25.0, 39.6, 68.7, 69.1, 83.0. NMR data are in agreement with those in the literature [89].

2,2′-(Buta-1,3-diyne-1,4-diyl)bis(adamantan-2-ol) (4e). Obtained from 2-ethynyladamantan-2-ol **3e** (175 mg, 0.994 mmol). White solid, m.p. 240–242 °C, yield 124 mg (71%). ^{1}H NMR (acetone-d_6, 400.1 MHz): δ 1.48–1.53 (m, 4H), 1.70–1.80 (m, 12H), 1.87–1.92 (m, 4H), 2.03–2.08 (m, 4H, 3CH), 2.16–2.23 (m, 4H), 2.97 (s, 2H, 2OH). $^{13}C\{^1H\}$ NMR (acetone-d_6, 100.6 MHz): δ 27.57, 27.64, 32.0, 35.8, 38.1, 39.3, 69.0, 72.6, 85.2. HRMS (ESI-TOF): m/z [M-OH]$^+$ Calcd for $C_{24}H_{29}O^+$: 333.2213; found: 333.2223.

2,7-Bis(4-chlorophenyl)octa-3,5-diyne-2,7-diol (4f). Obtained from 2-(4-chlorophenyl)but-3-yn-2-ol **3f** (181 mg, 1 mmol). Yellow-brown oil, yield 115 mg (64%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 1.77 (s, 6H, 2CH_3), 2.62 (s, 2H, 2OH), 7.32 (d, 4H, 4CH, *J* = 8.6), 7.53 (d, 4CH, *J* = 8.6). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 32.9, 69.0, 70.0, 82.9, 126.3, 128.6, 133.9, 142.9. NMR data are in agreement with those in the literature [90].

Dimerization of terminal acetylene 3a in gram scale**.** A 50 mL round-bottomed flask was charged with 2-methylbut-3-yn-2-ol **3a** (1684 mg, 20.05 mmol), MeOH (60 mL), TMEDA (6.4 mL, 44 mmol), CCl_4 (5 mL, 50 mmol) and CuCl (20 mg, 2 mmol were added at stirring by a magnetic stirrer). The reaction mixture was stirred for 1 day; volatiles were evaporated in vacuo. The residue was dispersed between 0.1 M of HCl (30 mL) and CH_2Cl_2 (20 mL). The organic layer was separated; the water phase was extracted by CH_2Cl_2 (20 mL). The combined organic phase was washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated in vacuo; the residue formed was by passing through a short

silica gel pad of silica gel using gradient eluation by CH_2Cl_2, followed by CH_2Cl_2-MeOH mixture (30:1). White powder, m.p. 124–126 °C, yield 1420 mg (85%). 1420 mg (85%). For NMR spectral data see above.

Dimerization of phenylacetylene 1a in the presence of TEMPO. An 8 mL vial with a screw cap was charged with phenylacetylene **1a** (57 mg, 0.56 mmol), MeOH (1.5 mL), TMEDA (0.16 mL, 1.1 mmol), CCl_4 (79 mg, 0.51 mmol), TEMPO (77 mg, 0.49 mmol) and CuCl (5.2 mg, 0.052 mmol), which were added at stirring by a magnetic stirrer. The reaction mixture was stirred for 1 day and then broken by 0.1 M of HCl (30 mL). The product was extracted by CH_2Cl_2 (3 × 10 mL); the organic phase was washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated in vacuo; the residue formed was purified by passing through a short silica gel pad of silica gel using gradient eluation by hexane, followed by hexane-CH_2Cl_2 mixture (3:1). White powder, yield 16 mg (28%). For NMR spectral data see above.

Dimerization of phenylacetylene 1a in the presence of α-cyclopropylstyrene. An 8 mL vial with a screw cap was charged with phenylacetylene **1a** (107 mg, 1.05 mmol), MeOH (3 mL), TMEDA (0.32 mL, 2.2 mmol), CCl_4 (174 mg, 1.13 mmol), α-cyclopropylstyrene (155 mg, 1.07 mmol) and CuCl (9 mg, 0.09 mmol), which were added at stirring by a magnetic stirrer. The reaction mixture was stirred for 1 day and then broken by 0.1 M of HCl (30 mL). The product was extracted by CH_2Cl_2 (3 × 10 mL); the organic phase was washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated in vacuo; the residue formed was purified by passing through a short silica gel pad of silica gel using gradient eluation by hexane, followed by hexane-CH_2Cl_2 mixture (3:1). White powder, yield 76 mg (72%). For NMR spectral data see above. Compound **6** was observed in the NMR spectra of crude product **2a**. The yield of **6** was calculated by comparison with the amount of 2a in the 1H NMR of crude 2a. The NMR data of **6** are in agreement with those in the literature [14].

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/catal13101330/s1, Copies of all NMR spectra.

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