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Chemo- and Regioselective Dimerization of Terminal Alkynes Promoted by Methylaluminoxane

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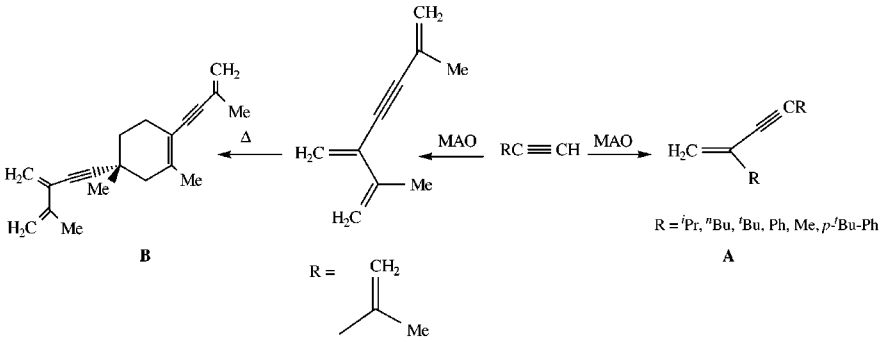
ABSTRACT



Methylalumoxane (MAO) was found to be an active catalytic precursor for the chemo- and regioselective dimerization of a wide range of aryl- and alkyl-substituted terminal alkynes yielding the corresponding geminal dimers A. For an olefin-functionalized terminal alkyne (RC≡CH, R = MeC═CH_2), the geminal dimer undergoes an intermolecular [4 + 2] cycloaddition forming compound B.

The metal-catalyzed dimerization/oligomerization of terminal alkynes attracts major research attention because it provides a facile entry into the chemistry of conjugated enynes, a versatile building block for the synthesis of natural products[1] and organic conducting polymers.[2] Enynes are the simplest coupling product of alkynes in the metal-based oligomerization cycle. The catalytic dimerization cycle is believed to proceed by the activation of the alkyne C−H bond by a metal complex producing the metal acetylide LnMC≡CR (Ln = ancillary ligands) compound. Insertion of the alkyne carbon−carbon triple bond into the acetylide moiety yields an alkenyl intermediate LnMCH═CRC≡CR, which may followed by a σ-bond metathesis with another alkyne C−H bond, allowing the dimer formation and regenerating the LnMC≡CR species. The factors that govern the regio- and stereoselectivity strongly depend on the electronic and steric hindrance of the alkyne substituents and the coordination sphere of the active metal center.[3] The use of stoichiometric amounts of organoaluminum reagents in organic synthesis is well documented in the literature.[4] Regarding the catalytic use of organoaluminum compounds, they have been utilized in processes such as hydrosilylation reactions,[5] epoxide ring opening to carbonyl compounds [6] and recently in the polymerization of α-olefins.[7] Regarding alkynes, a bis-(benzamidinate) aluminum hydride complex[8] and, recently, a cationic aminotroponiminate aluminum complex[9] have been found to promoted the selective dimerization of ^{t}BuC≡CH

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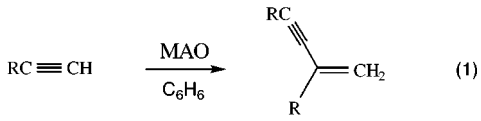
toward the corresponding geminal dimer. For other group 13 metal compounds, the linear trimerization of silylacetylene has been observed, using $GaCl_3$ in the presence of Grignard reagents.[10] In this paper, we report the catalytic activity of methylaluminoxane (MAO), the well-known cocatalyst in the polymerization of α-olefins, for the regio- and chemoselective head-to-tail dimerization of terminal alkynes. In addition, we present a simple kinetic competition between two different alkynes allowing the formation of cross dimers.

Moreover, we show that the head-to-tail dimer obtained from the dimerization of the vinyl substituted alkyne HC≡C−C(Me)=CH_2, undergoes either an intermolecular Diels−Alder cycloaddition, or reacts with the polar alkyne HC≡CCO_2Et to form the corresponding Diels−Alder cross adduct.

Reaction of an excess of ^{i}PrC≡CH with catalytic amounts of methylaluminoxane (MAO), in nonpolar solvents (C_6H_6, toluene, cyclohexane), results in the exclusive multigram formation of the chemo- and regioselective head-to-tail dimer 2,4-diisopropyl-1-butene-3-yne (**1**), without formation of other dimer or higher oligomers. To explore the scope of the catalytic reaction, the dimerization reactions on a range of substrates (alkyl- and aryl-substituted terminal alkynes) were studied under similar reaction conditions producing, in all cases, exclusively the corresponding regioselective head-to-tail dimer as shown in eq 1 (Table 1).



(1)

R = ^{i}Pr (**1**); ^{n}Bu (**2**); ^{t}Bu (**3**); Ph (**4**); Me (**5**); *p*-^{t}Bu-Ph (**6**)

The dimerization of terminal alkynes was found to be slow at room temperature depending on the nature of the alkyne substituents. For example, for ^{t}BuC≡CH, 10 days are necessary at room temperature to complete a 100% conversion into the corresponding geminal dimer in quantitatively yield (> 99%), whereas for other less bulky substituted terminal alkynes the time varies from 20 h up to 48 h. In contrast, when the reaction was carried out at higher temperature (78 °C), 99.5% yield was obtained for almost all alkynes in about 1 h (Table 1).

Table 1. Activity Data for the Catalytic Dimerization of Teminal Alkynes (RC≡CH) Promoted by Methylaluminoxane[a]

entry	R	solvent[b]	*gem*-H_2C=C(R)C≡C(R) (isolated yield, %)	N_t, h^{-1} [c]
1	^{i}Pr	C_6H_6	99.3	5.1
2	^{n}Bu	C_6H_6	99.2	4.8
3	^{t}Bu	C_6H_6	99.7	0.4
4	Ph	C_6H_6	99.4	3.7
5	Me	C_6H_6	97.4	0.1
6	p-^{t}Bu−Ph	C_6H_6	99.1	3.3
7	H_2C=C(Me)	C_{6H6}	99.2	2.4
8	Me_3Si[d]	C_6H_6	44[e]	0.1
9	^{i}Pr	toluene	98.9	4.4
10	^{i}Pr	cyclohexane	99	1.5
11	^{i}Pr[f]	THF		
12	^{i}Pr[f]	diethyl ether		
13	^{i}Pr	no solvent	99.5	4.7

[a] The reactions were carried out at the corresponding reflux temperatures. [b] Deuterated solvents. [c] Turnover frequencies. [d] No reaction was observed at room temperature. [e] Other dimers are obtained in the reaction mixture: *trans*-(TMS)CH=CHC≡C(TMS) (33%) and *cis*-(TMS)CH=CHC≡C(TMS) (23%). [f] No reaction was observed at either room or reflux temperatures.

The activation parameters for the MAO-dimerization of ^{i}PrC≡CH were measured and are characterized by a rather small enthalpy of activation (11.6(3) kcal mol^{-1}) and a large negative (even for an intermolecular reaction) entropy of activation (−40.4(5) eu; $\Delta G^{\ddagger} = 24(1)$ kcal mol^{-1} at 298 K). These parameters suggest a highly ordered transition state with considerable bond making to compensate to bond breaking. Thus, it seems plausible that a four-center transition state is operative for aluminum complexes in analogy to other early transition-metal/lanthanide/actinide complexes, were no oxidative addition or reductive elimination operative exhibiting a large negative entropy of activation (Figure 1). [11]

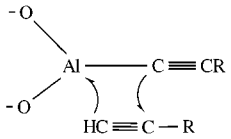
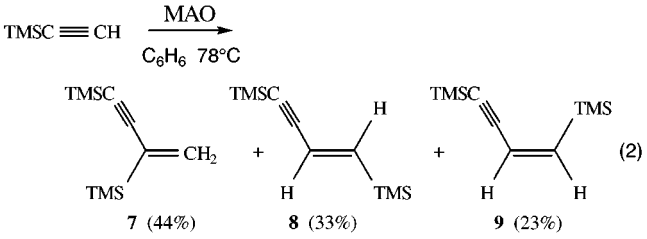


Figure 1. Plausible mode of insertion for organoaluminum complexes.

In contrast to the alkyl- and aryl-substituted alkynes, the dimerization reaction of TMSC≡CH was found to proceed without selectivity. The catalytic reaction with MAO is operative only at high temperatures producing a mixture of the three expected dimers (the number in parentheses are the isolated yields with a conversion of 100%) (eq 2).[12,13]



(2)

The solvent effect was also studied in the MAO-catalyzed dimerization of ^{i}PrC≡CH. For aromatic solvents like C_6H_6 or toluene, no major difference is exhibited in the kinetics of the reaction. In cyclohexane, the reaction is slower by a factor of 3 possibly because of the low miscibility of MAO in nonpolar aliphatic solvents. However, no reaction was observed in polar solvents (ether, THF), presumably due to

(5) (a) Asao, N.; Sudo, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 7654. (b) Sudo, T.; Asao, N.; Gevorgyan, V.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2494.

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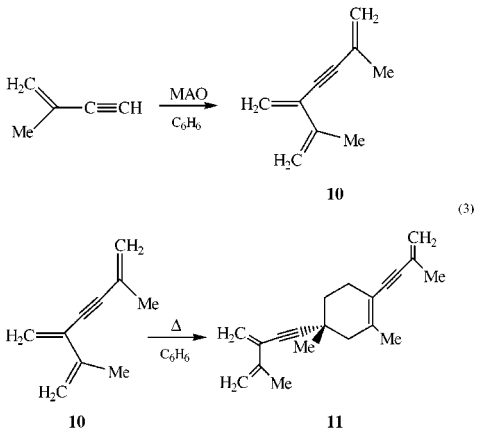
the coordination of the donor atom of the solvent to the Lewis acid metal center. This interaction is expected to block the coordination site at the metal impeding the alkyne to react with either an Al-Me or an Al-acetylide moiety. The same lack in reactivity was observed by using substituted terminal alkynes containing heteroatom functional groups (RC≡CH; R = CH_2NH_2, CH_2NMe_2, CO_2Et, CH_2CH_2CN).

Although the turnover frequencies for the MAO-catalyzed dimerization of terminal alkynes are rather small (Table 1), in the absence of moisture and oxygen, MAO is able to react continuously producing large turnover numbers (50−100). Hence, the reaction of MAO with ^{i}PrC≡CH (1:10) was carried out repeatedly 10 times with the same catalyst, after vacuum transferring the product, indicating a high thermal and chemical stability of the active Al complex. Unlike the heteroatom-substituted terminal alkynes, the olefin functionalized terminal alkyne undergoes coupling reaction toward the head-to-tail dimer. Thus, the reaction of MAO in benzene with an excess of HC≡CC(Me)=CH_2 results in the quantitative formation of the geminal dimer **10** in 20 or 2 h at either room temperature or 78 °C, respectively (eq 3).[14]



10 **10** **11** (3)

Heating a benzene solution of compound **10** (78 °C for 5 h) leads to the quantitative (yield >99.5%) formation of **11**, which is the [4 + 2] intermolecular Diels−Alder cycloaddition product. From the two possible expected stereoisomers, only one isomer was exclusively obtained as established by 2D-NMR spectroscopic measurements.[14,15] It is noteworthy that small or trace amounts of higher cycloaddition oligomers where not detected by either NMR or GC/MS spectrometry.

To study the fate of the MAO during the reaction, a stoichiometric reaction between MAO and deuterated alkyne ^{i}PrC≡CD was studied. Mixing MAO with ^{i}PrC≡CD at room temperature in a stoichiometric ratio of 1:2, respectively, allows the formation of CH_3D and the dideuterium geminal dimer D_2C=C(^{i}Pr)C≡CPr^i, suggesting the formation of an aluminum−acetylide bond. The CH_3D was characterized by either ^{2}H NMR (δ = −1. 43 ppm) or ^{13}C{H} NMR (δ = 14.1, doublet, ^2J = 18.8 Hz). Kinetically, by comparing the reaction of MAO with either ^{i}PrC≡CD or ^{i}PrC≡CH, no kinetic isotope effect was observed, indicating the rapidity of the reaction. Moreover, the stoichiometric reaction of MAO with ^{i}PrC≡CH (1:2) yielded at room temperature only the geminal dimer despite the possible formation of 4-methyl-2-pentene or 2,3-dimethyl-1-butene isomers. This result corroborates that for MAO, the insertion of the alkyne into the Al−alkyl bond is not a major competing pathway for product formation.[4b,16]

To gain some insight into the catalytic reaction and to understand the role of the aluminum center in MAO (to ensure that no other metal contamination is the active catalyst), a similar reaction was carried out utilizing Me_3Al instead of MAO. Thus, in the reaction of Me_3Al with ^{i}PrC≡CH at room or high temperature no products are observed. However, the addition of a stoichiometric amount of triple distilled water (Me_3Al/H_2O = 1:1.8) into the same reaction mixture leads to a quantitative formation of the head-to-tail dimer **1**. This result corroborates with the fact that MAO is a stronger Lewis acid as compared to Me_3Al and is presumably responsible for such activity.[17,18]

A plausible pathway for the MAO-catalyzed dimerization of terminal alkynes is shown in Scheme 1. The proposed mechanism consists of a sequence of well-established elementary reactions such as insertion of an alkyne into an M−carbyl σ-bond and σ-bond metathesis. Thus, the first step in the catalytic cycle involves the σ-bond metathesis

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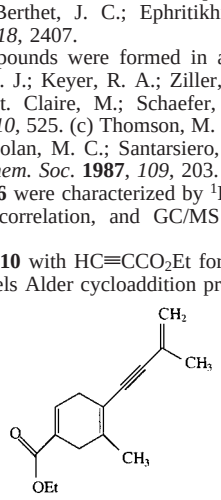
(12) Stockis and Hoffmann have performed calculations on the polarization of the π*-orbitals in TMSC≡CH. The electronic effects due to the polarization are believed to be responsible for the difference in regioselectivities of the dimerization results. Stockis, A.; Hoffmann, R. *J. Am. Chem. Soc.* **1980**, *102*, 2952. The cis isomer will probably be formed by an isomerization of the trans isomer via an envelope mechanism; see: Wang, J. Q.; Dash, A. K.; Berthet, J. C.; Ephritikhine, M.; Eisen, M. S. *Organometallics* **1999**, *18*, 2407.

(13) No allenic compounds were formed in any of the dimerization reactions. (a) Evans, W. J.; Keyer, R. A.; Ziller, J. W. *Organometallics* **1993**, *12*, 2618. (b) St. Claire, M.; Schaefer, W. P.; Bercaw, J. E. *Organometallics* **1991**, *10*, 525. (c) Thomson, M. E.; Baxter, S. M.; Bulls, A. R.; Burger, B. J.; Nolan, M. C.; Santarsiero, B. D.; Schefer, W. P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 203.

(14) Compound **1**−**16** were characterized by ^{1}H NMR, ^{13}C NMR, 2D-COSY, NOESY, CH correlation, and GC/MS spectroscopy; see the Supporting Information

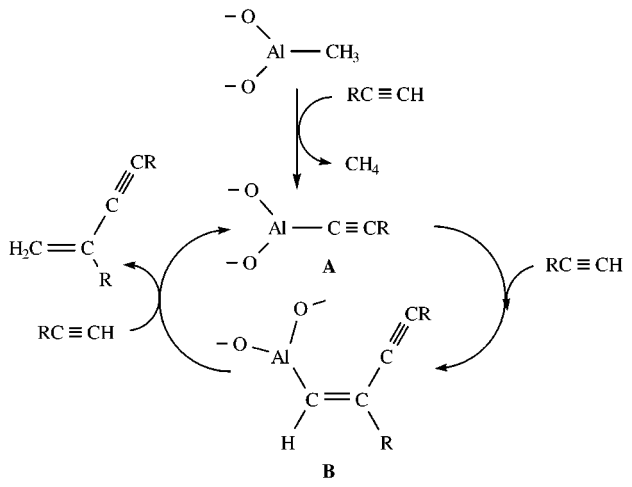
(15) The reaction of **10** with HC≡CCO_2Et for 5 h at 78 °C forms **11** (78%) and the cross Diels Alder cycloaddition product **16** (22%).



16

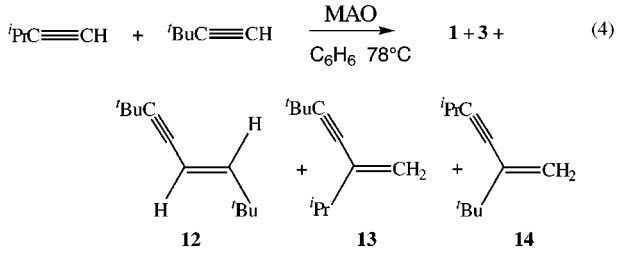
(16) The insertion reaction of alkynes into Al−R (R= ethyl, isobutyl) or Al−H producing the corresponding Al−vinyl bond has been reported; see: Wilke, G. V.; Müller, H, *Liebiegs Ann. Chem.* **1960**, *629*, 222.

Scheme 1. Plausible Mechanism for the Dimerization of Terminal Alkynes



between the terminal C−H bond of the alkyne and the Al−Me bond of MAO, yielding the rapid formation of the acetylide complex AlC≡CR (**A**) and methane, as observed during the catalytic and stoichiometric reactions. Complex **A** undergoes a regioselective 1,2-head-to-tail insertion (through a four-center transition state), yielding the alkenyl complex **B**. The protonolysis of complex **B**, by another alkyne, produces the corresponding geminal dimer and regenerates the catalytic complex **A**. As no higher oligomers are observed during the catalytic reaction, the turnover limiting step for the catalytic dimerization is the insertion of the alkyne into the Al−acetylide complex.[19]

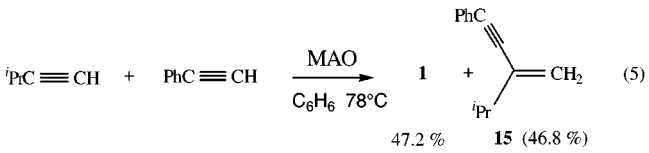
Since in the dimerization of the terminal alkynes only the geminal dimers were produced, it was interesting to induce some kinetic competition to allow the formation of specific cross dimers. The reaction of equimolar amounts of ^{i}PrC≡CH and ^{t}BuC≡CH with MAO produced, after 12 h, three homocoupling and two cross-coupling dimers (eq 4). The obtained homocoupling dimers were the expected **1** and **3** and trace amounts of the unexpected trans isomer **12**, which is formed by the insertion of ^{t}BuC≡CH into the *tert*-butyl acetylide complex when the bulky group of the alkyne is pointing toward the metal center (Figure 1). The cross dimers obtained were the two geminal **13** and **14**, resulting from the regioselective insertion of ^{i}PrC≡CH into the *tert*-butyl acetylide complex and from the regioselective insertion of ^{t}BuC≡CH into the isopropyl acetylide complex, respectively (eq 4). The different amounts of **13** and **14** suggest that the insertion of ^{i}PrC≡CH into either the isopropyl-acetylide or the ^{t}butyl-acetylide metal complex is much faster than that of the bulkier ^{t}BuC≡CH. To support the insertion hypothesis,



*i*PrC≡CH/*t*BuC≡CH	time, h	**1** (%)	**3** (%)	**12** (%)	**13** (%)	**14** (%)
1:1	12	34.2	28.9	1.5	28.0	6.5
1:1	2	60.6	2.8		30.6	6.0
2:1	12	64.0	8.7		22.6	4.7
1:2	0.5	40.9	6.5		43.5	9.2

three parallel reactions were carried out. In the first reaction, the cross dimerization products were followed at regular intervals during the course of the reaction using equimolar amounts of the two alkynes, whereas the other two experiments were performed by using nonequimolar ratio between the alkynes. The reaction of equimolar amounts of ^{i}PrC≡CH and ^{t}BuC≡CH with MAO was stopped after 2 h (time to complete the exclusive disappearance of ^{i}PrC≡CH), producing **1**, **13** as the major cross compound, and **14**. Similarly, the dimerization of a 2:1 or 1:2 ratio of ^{i}PrC≡CH/^{t}BuC≡CH for 12 or 0.5 h, respectively, corroborates for a faster insertion of the ^{i}PrC≡CH into the metal-acetylide as compared to ^{t}BuC≡CH (eq 4).

Interestingly, the cross dimerization of a 2:1 ratio of ^{i}PrC≡CH and PhC≡CH produced nearly the same amounts of **1** and the cross dimer **15** with a total yield of 94%. The latter is obtained by the insertion of ^{i}PrC≡CH into the phenylacetylide−aluminum bond (eq 5).



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Supporting Information Available: Experimental procedures and ful spectroscopic data for compounds **1**−**16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) Zirconocene dimethyl will react with MAO yielding the corresponding cationic zirconocene complex, whereas Me_3Al is unable to remove the methyde group (methyl with the pair of electrons) from the metal center.

(18) Attempts to trap any organoaluminium complexes in situ by NMR spectroscopy were unsuccessful.

(19) In the hydrosilylation of alkynes catalyzed by AlX_3 or $RAlCl_2$, the zwiterionic complex **I** has been proposed. For MAO, this intermediate can be ruled out because of the following observations: The hydrosilylation of terminal alkynes with $PhSiH_3$ by MAO does not occur and a stoichiometric amount of $PhSiH_2Me$ was obtained. No reaction was observed for internal alkynes, as already observed for complex **I**.[5] No reaction was observed for terminal alkynes with functional electron-withdrawing groups.