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A General Study of Aryloxo and Alkoxo Ligands in the Titanium-Catalyzed Intermolecular Hydroamination of Terminal Alkynes

Annegret Tillack,[a] Vivek Khedkar,[a] Haijun Jiao,[a] and Matthias Beller*[a]

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A general study of the regioselective hydroamination of terminal alkynes in the presence of $Ti(NEt_2)_4$ and different aryloxo and alkoxo ligands is presented. Depending on the ligand the regioselectivity towards the Markovnikov and the *anti*-Markovnikov addition product can be controlled. The experimentally observed isomer distribution is explained perfectly by detailed theoretical investigations which demonstrate that the regioselectivity is determined by the relative stability of the corresponding alkynetitanium π complexes.

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Introduction

The addition of nitrogen and oxygen compounds across carbon–carbon multiple bonds is an important subject in organic synthesis.[1] In general, these processes are perfectly suited to fulfil today's requirements for sustainable processes because of the availabilty of substrates, and 100% atom efficiency. By using unsymmetrical olefins or alkynes the addition of H–Nu (Nu = OR, NR_2, etc.) can lead to two isomeric products. Typically, most of the electrophilic addition reactions follow the Markovnikov rule, in which the branched compound is mainly produced. However, often the linear isomer is the more desired product for industrial bulk applications. Hence, *anti*-Markovnikov functionalizations, especially of aliphatic olefins, continue to be a challenging goal for catalysis.

It is obvious that the introduction of tailor-made transition metal complexes led to significant advances over the last decades in a number of functionalization reactions, e.g. hydroformylation, hydrocarboxylation, hydrocyanation. Nevertheless, control of chemo-, regio- and enantioselectivity for addition processes to unsaturated substrates needs to be further improved, because this is the basis for new applications and innovation in organic synthesis.

We have been involved in the development and exploration of new methods for selective amination of olefins and alkynes for some time now. Apart from carbonylative amination of olefins (so-called hydroaminomethylations),[2] the direct hydroamination of olefins[3] and alkynes has attracted our interest. Over the last decade a multitude of catalysts have been explored for alkyne hydroaminations.[4] Because of their reactivity and availability titanium complexes have probably attracted the most interest. Important progress in the intermolecular hydroamination of alkynes with titanium complexes has been reported by Bergman,[5] Doye,[6] Odom,[7] us,[8] Schafer,[9] and others.[10] It is worth noting that Ackermann et al. recently demonstrated that norbornene reacts with various anilines in the presence of $TiCl_4$.[10d]

Among the various titanium catalysts that are known for hydroamination, we introduced bis(aryloxo)-bis(dialkylamido)titanium complexes, which are comparably air-stable and easy to handle. These complexes catalyze the selective Markovnikov hydroamination of terminal alkynes.[11] Recently, we also reported that by addition of different phenol ligands to $Ti(NEt_2)_4$ the regio- and chemoselectivity of hydroaminations of terminal alkynes can be controlled.[12] Here, we present a full account of our selectivity studies. Furthermore, we present theoretical calculations, which explain the observed selectivity.

Results and Discussion

Monodentate Alkoxo and Aryloxo Ligands in Hydroamination of Alkynes

Recently, we investigated the control of regioselectivity (Markovnikov or *anti*-Markovnikov) by using titanocene catalysts with different ligands in the hydroamination of unsymmetrical alkynes (Scheme 1).[8a]

Based on this work we were interested in investigating, in more detail, the influence of monodentate and bidentate alkoxo and aryloxo ligands on the regioselectivity of the intermolecular hydroamination of terminal alkynes. Initially, the addition of *sec*-butylamine to 1-octyne was studied as a model reaction in the presence of 11 monodentate alkoxo and aryloxo ligands (Table 1). With regards

[a] Leibniz-Institut für Organische Katalyse an der Universität Rostock e.V.,
Albert-Einstein-Str. 29a, 18059 Rostock, Germany
Fax: +49-381-1281-5000
E-mail: matthias.beller@ifok-rostock.de

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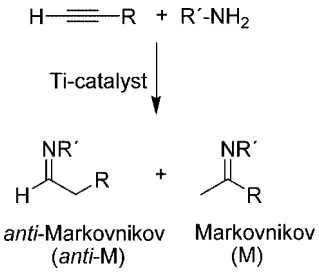
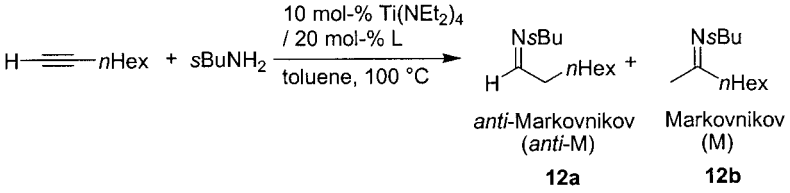


Scheme 1. Hydroamination of terminal alkynes.

to practicalities, instead of using synthesized alkoxo- or aryloxotitanium complexes, we formed the corresponding titanium catalysts in situ from commercially available $Ti(NEt_2)_4$ and alcohols or phenols **1**–**11** (Scheme 2). In general, the hydroamination reaction was performed in toluene at 100 °C for 24 h in the presence of 10 mol-% $Ti(NEt_2)_4$ and 20 mol-% of the corresponding ligand. Typically a slight excess of amine (1:1.2 equiv.) was employed in order to suppress oligomerization and polymerization of 1-octyne. Nevertheless, small amounts of dimers, oligomers and polymers of the alkyne and also amine-alkyne dimers were observed in the case of the less selective catalysts.

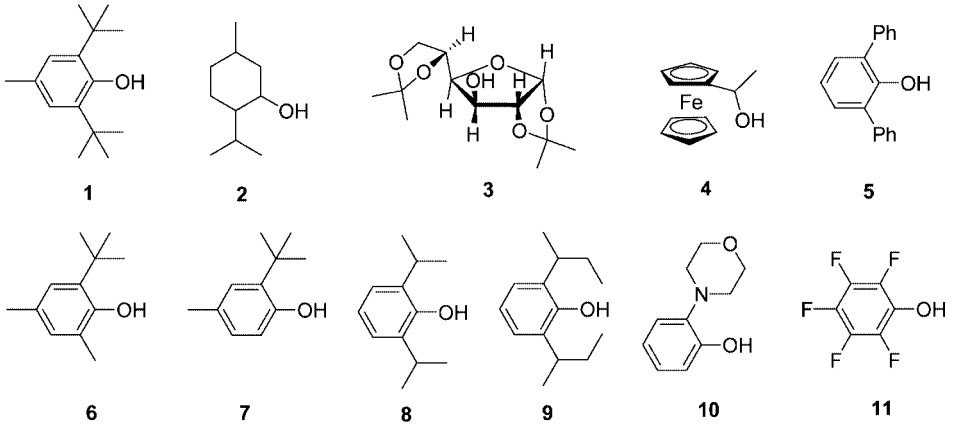
In a preliminary study[12] we have shown that the use of sterically hindered bulky phenol **1** in the hydroamination of 1-octyne with *sec*-butylamine gave an excellent yield (98%) and a high Markovnikov selectivity (*anti*-M:M = 10:90). However, by employing sterically hindered alkoxo ligands **2**

Table 1. Hydroamination of 1-octyne with *sec*-butylamine in the presence of $Ti(NEt_2)_4$/ligand.[a]



Entry	Ligand	Conversion [%]	Yield[b] [%]	*anti*-M:M ratio[c]
1	**1**	100	98	10:90
2	**2**	66	64	74:26
3	**3**	14	13	76:24
4	**4**	32	31	75:25
5	**5**	100	97	49:51
6	**6**	100	88	72:28
7	**7**	100	94	94:6
8	**8**	100	97	94:6
9[d]	**8**	100	98	94:6
10[e]	**8**	83	82	96:4
11	**9**	100	98 (70)	94:6 (96:4)
12	**10**	100	90	95:5
13	**11**	7	4	84:16

[a] Reaction conditions: 1.5 mmol 1-octyne, 1.8 mmol amine, 10 mol-% catalyst, Ti/L = 1:2, 2 mL toluene, 100 °C, 24 h. [b] Yield is determined by GC analysis with dodecane or hexadecane as internal standard, isolated yield is given in parenthesis. [c] GC analysis used to determine the regioisomers, the ratio of regiomers of the isolated product after distillation is given in parenthesis. [d] 85 °C. [e] 5 mol-% catalyst.



Scheme 2. Alkoxo and aryloxo monodentate ligands used in our study.

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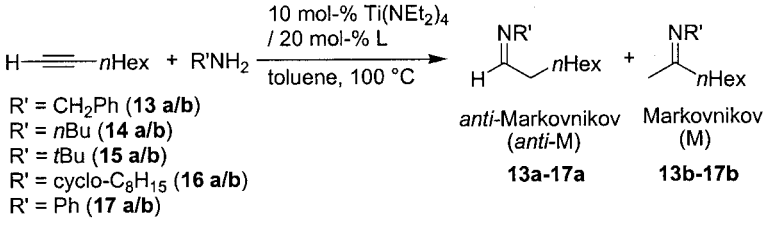
and **3** a lower yield of the corresponding imines with poor regioselectivity was obtained (Table 1, Entries 2–3). Also in the presence of ferrocenyl ligand **4** (benzyloxo type) hydroamination proceeded very slowly and gave only a 31% yield of the corresponding imines (Table 1, Entry 4). Compared to alkoxo and benzyloxo ligands, monodentate phenols gave good to excellent conversions and yields of the corresponding imine. Surprisingly, when using 2,6-diphenlyphenol (**5**) the selectivity dropped significantly and a 1:1-mixture of regioisomers was obtained. In the presence of 2-*tert*-butyl-4,6-dimethylphenol (**6**) an 88% yield of imines was obtained with major *anti*-Markovnikov selectivity (*anti*-M:M = 72:28).

Excellent *anti*-Markovnikov selectivity (94:6 to 95:5) is observed in the presence of ligands **7**, **8**, **9** and **10**. Thus, a switch from the Markovnikov product to the *anti*-Markovnikov product is observed simply by changing the phenol ligand from **1** to **8**, **9** or **10**. Here, especially the behavior of the 2-morpholinophenol (**10**) is surprising. To the best of our knowledge this is the first example where aminophenol is used as a ligand in titanium-catalyzed aminations.

In general, only sterically hindered phenols showed significant catalytic activity. By employing simple phenol or pentafluorophenol **11** as the ligand no activity was observed due to the formation of stable tris- and tetrakisphenoxo titanium complexes (Table 1, Entry 13).

Next, we were interested in the generality of the observed regioselectivity effect (Table 2). Hence, the behavior of ligands **1**–**2** and **5**–**10** was tested in the hydroamination reaction of 1-octyne with benzylamine, *n*-butylamine, *tert*-butylamine, cyclooctylamine and aniline. In the presence of ligand **1** excellent yields of the imines and a high Markovnikov selectivity was obtained with nonhindered amines such as benzylamine, *n*-butylamine, cyclooctylamine and aniline

Table 2. Hydroamination of 1-octyne with different amines using $Ti(NEt_2)_4$ and monodentate ligands.[a]



Entry	Ligand	Amine	Conversion [%]	Yield[b] [%]	*anti*-M:M ratio[c]
1	**1**	benzylamine	100	99	20:80
2	**1**	*n*-butylamine	100	99	25:75
3	**1**	cyclooctylamine	100	99	14:86
4	**1**	*tert*-butylamine	50	50	74:26
5[d]	**1**	*tert*-butylamine	75	58	88:12
6	**1**	aniline	100	99	22:78
7[d]	**1**	aniline	100	96	20:80
8	**2**	benzylamine	12	9	44:56
9	**2**	*tert*-butylamine	26	22	92:8
10	**5**	benzylamine	92	86	43:57
11	**5**	*n*-butylamine	100	96	48:52
12	**5**	*tert*-butylamine	23	18	74:26
13	**5**	aniline	100	98	16:84
14[e]	**5**	aniline	100	40	30:70
15	**6**	benzylamine	97	44	70:30
16	**6**	*tert*-butylamine	22	20	92:8
17	**7**	benzylamine	100	52	84:16
18	**7**	cyclooctylamine	100	92	94:6
19	**7**	*tert*-butylamine	98	66	99:1
20	**8**	benzylamine	100	72 (41)	86:14 (87:13)
21	**8**	*n*-butylamine	100	82	92:8
22	**8**	cyclooctylamine	100	94 (65)	94:6 (96:4)
23	**8**	*tert*-butylamine	54	44	99:1
24	**8**	aniline	100	86 (37)	34:66 (30:70)
25	**9**	benzylamine	100	70	88:12
26	**9**	*n*-butylamine	100	88 (50)	91:9 (91:9)
27	**9**	*tert*-butylamine	33	30	99:1
28	**10**	benzylamine	98	40	93:7
29	**10**	*tert*-butylamine	89	49	98:2

[a] Reaction conditions: 1.5 mmol 1-octyne, 1.8 mmol amine, 10 mol-% catalyst, Ti/L = 1:2, 2 mL toluene, 100 °C, 24 h. [b] Yield is determined by GC analysis with dodecane or hexadecane as internal standard, isolated yield is given in parenthesis. [c] GC analysis was used to determine the regioisomers, the ratio of regiomers of the isolated product after distillation is given in parenthesis. [d] Ti:L = 1:1. [e] $(2,6\text{-}C_6H_5\text{-}C_6H_3O)_2TiCl_2$ as catalyst; reaction conditions: 1.5 mmol 1-octyne, 1.5 mmol aniline, 0.9 mmol tBuNH$_2$ as additive, 10 mol-% catalyst, 2 mL toluene, 100 °C, 24 h.

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(Table 2, Entries 1–3 and 6–7). However, sterically hindered *tert*-butylamine gave only a low yield with a high *anti*-Markovnikov selectivity (Table 2, Entries 4–5).

When using ligand **2** the reaction with benzylamine gave a very low yield (9%) and a 1:1-mixture of regioisomers. Also *tert*-butylamine led to a low yield (22%), but with excellent *anti*-Markovnikov selectivity (*anti*-M:M = 98:2). When employing ligand **5** with different aliphatic amines the observed regioselectivity is bad (Table 2, Entries 10–12). The reaction of aniline, using the in situ formed aryloxotitanium complex from commercially available $Ti(NEt_2)_4$, and **5** gave an excellent yield (98%) with predominant Markovnikov selectivity (Table 2, Entry 13). At this point it is interesting to note that previous studies showed that the reaction of anilines with internal alkynes using simple $TiCl_4$ as the catalyst gave less of the hydroaminated product (<2%). However, Ackermann demonstrated that the catalytic activity for such a reaction can be increased by addition of *tert*-$BuNH_2$ (up to 96%).[10e] Thus, we also tested the defined complex $(2,6\text{-}C_6H_5\text{-}C_6H_3O)_2TiCl_2$ in the presence of *tert*-butylamine as the additive, as well as without this additive. Here, a 40% yield of imine is obtained with the additive (Table 2, Entry 14) (without additive <1%), which is less efficient compared to the halide-free aryloxotitanium complex. The hydroamination reaction using different aliphatic amines in the presence of ligands **6**–**10** gave preferentially the *anti*-Markovnikov product with good to excellent selectivity (*anti*-M:M = 70:30 to 99:1). However, in the case of aniline a high Markovnikov selectivity was obtained by employing **8** (Table 2, Entry 24).

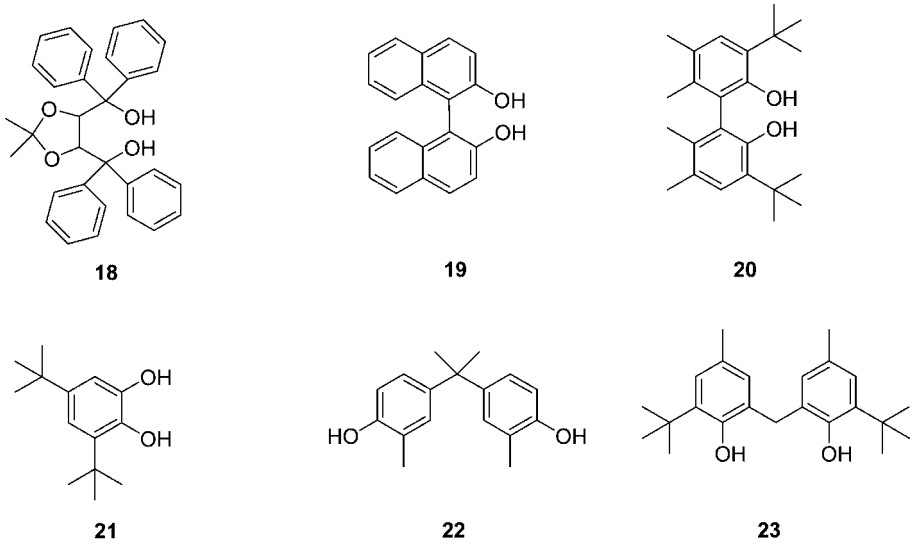
In general, the ligand has a significant impact on the observed selectivity. However, the nature of the amine also influences the regioselectivity and yields of the corresponding imines. For example the reaction with sterically hindered *tert*-butylamine in the presence of all the tested ligands proceeds very slowly with a high *anti*-Markovnikov selectivity. On the other hand when applying aniline, the Markovnikov isomer is always obtained preferentially. A more detailed discussion of this selectivity effect is presented in the area of theoretical investigations (see below).

Bidentate Alkoxo and Aryloxo Ligands in Hydroamination of Alkynes

Next, we investigated the effect of bidentate alkoxo and aryloxo ligands (Scheme 3) in different titanium-catalyzed hydroamination reactions. Here, we performed the hydroamination of 1-octyne with six different alkoxo and aryloxo ligands (**18**–**23**) with simple nonhindered amines, e.g. benzylamine, *sec*-butylamine and sterically hindered *tert*-butylamine (Table 3).

The reaction of benzylamine in the presence of bidentate ligands **18**–**23** led preferentially to the Markovnikov imines, albeit with somewhat lower selectivity (*anti*-M:M = 40:60 to 28:72) and very low yields (10–52%). Surprisingly, *sec*-butylamine led preferentially to the *anti*-Markovnikov isomer. Applying this amine compared to benzylamine the yields of the corresponding imines were good (Table 3, Entries 2, 5, 8, 11 and 15), except for ligand **22** because of the precipitation of the Ti complex (Table 3, Entry 13). This result is in contrast with those from experiments in the presence of monodentate ligands for nonhindered amines.

As expected *tert*-butylamine reacted slowly in the presence of ligands **18**, **19** and **23** with low yields and high *anti*-Markovnikov selectivity. However, a bulky group on the *ortho*-position of bidentate phenols **20** and **21** led to good yields of imines with excellent *anti*-Markovnikov selectivity (74–88%, *anti*-M:M = 97:3 to 99:1). In general, when applying bidentate phenol ligands, oligomers and polymers of 1-octyne were observed as side products.



Scheme 3. Bidentate alkoxo and aryloxo ligands used in catalytic hydroamination reactions.

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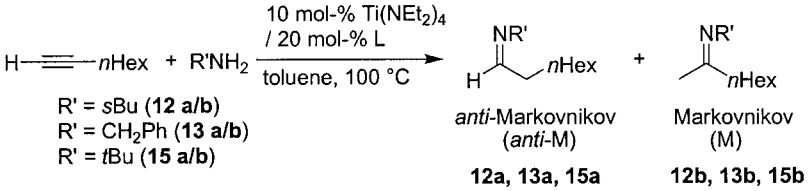
Table 3. Hydroamination of 1-octyne with different amines using $Ti(NEt_2)_4$ and bidentate ligands.[a]



Entry	Ligand	Amine	Conversion [%]	Yield[b] [%]	*anti*-M:M ratio[c]
1	**18**	benzylamine	14	10	33:67
2	**18**	*sec*-butylamine	72	63	68:32
3	**18**	*tert*-butylamine	46	39	98:2
4	**19**	benzylamine	81	52	33:67
5	**19**	*sec*-butylamine	100	88	62:38
6	**19**	*tert*-butylamine	100	36	86:14
7	**20**	benzylamine	52	30	30:70
8	**20**	*sec*-butylamine	90	88	56:44
9	**20**	*tert*-butylamine	97	86	97:3
10	**21**	benzylamine	91	48	28:72
11	**21**	*sec*-butylamine	100	91	76:24
12	**21**	*tert*-butylamine	100	74	99:1
13[d]	**22**	*sec*-butylamine	5	5	76:24
14	**23**	benzylamine	70	22	40:60
15	**23**	*sec*-butylamine	99	70	76:24
16	**23**	*tert*-butylamine	58	36	94:6

[a] Reaction conditions: 1.5 mmol 1-octyne, 1.8 mmol amine, 10 mol-% catalyst, Ti/L = 1:1, 2 mL toluene, 100 °C, 24 h. [b] Yield is determined by GC analysis with dodecane or hexadecane as internal standard. [c] GC analysis was used to determine the regioisomers. [d] Ti complex precipitates.

Comparison of Catalytic Systems

Next, we were interested in comparing the in situ generated catalyst from commercially available $Ti(NEt_2)_4$ and aryloxo ligand **1** with the previously described bis(2,6-di-*tert*-butyl-4-methylphenoxo)-bis(dimethylamido)titanium complex **24** in the hydroamination of 1-octyne with different amines. Catalytic experiments were performed with both systems at 100 °C for 24 h (Table 4).

By employing *n*-butylamine, benzylamine, *sec*-butylamine and cyclooctylamine, similar yields of the corresponding imine and almost similar regioselectiviy are observed with both catalytic systems (Table 4, Entries 1–8). Interestingly, the reaction of *tert*-butylamine with 1-octyne in the presence of the defined complex **24** did not work (Table 4, Entry 9). However, by using the in situ system [Ti-$(NEt_2)_4$/**1**] under the same reaction conditions the corresponding imine is obtained in 50% yield with high *anti*-Markovnikov selectivity (*anti*-M:M = 74:26) (Table 4, Entry 10). This effect might be explained by the formation of different $Ti(OAr)_n(NHtBu)_{4-n}$ species under the in situ conditions. In agreement with this the reaction of *tert*-butylamine in the presence of a 1:1-catalyst-to-ligand-ratio gave a better regioselectivity compared to a 1:2 ratio (Table 4, Entries 10 and 11). Also, by applying aniline the concentration of the ligand influenced the regioselectivity (Table 4, Entries 12 and 13). Thus, we were interested in studying the effect of the ligand concentration in more detail. Table 5 summarizes the influence of the titanium to ligand ratio (Ti/L) in the hydroamination of 1-octyne with *sec*-butylamine. Here, we used aryloxo monodentate ligands **1**, **5**, **7** and **8**, which have been proven to give the best regioselectivity with this amine in the hydroamination reaction. Using the in situ catalyst system $Ti(NEt_2)_4$/**1** a significant change in regioselectivity was observed by varying the Ti/L ratio from 1:1 to 1:2 (Table 5, Entries 1 and 2). Further increasing the ratio up to 1:4 (Ti/**1**) did not influence the regioselectivity (Table 5, Entry 3). The sterically less hindered ligands **5**, **7** and **8**, when compared to **1**, did not work at all when higher concentration of ligands were used (Table 5, Entries 6, 7, 10, and 14). All the ligands that were tested showed lower regioselectivity for the 1:1 ratio (Ti/L), and the best results were obtained for a 1:2 Ti/L ratio.

The influence of the ligand concentration is explained by the fact that the sterically hindered ligand **1** does not form tris- and tetrakis(aryloxo)titanium complexes at higher ligand ratios. However, tris- and tetrakis(aryloxo)titanium complexes were formed quickly by employing sterically less hindered ligands **5**, **7** and **8**.

Hydroamination of Internal Alkynes

We also studied the feasibility of aryloxo ligands in the hydroamination of an unsymmetrical internal alkyne. Here, the hydroamination reaction of methylphenylacetylene with benzylamine was performed using $Ti(NEt_2)_4$ and four different monodentate aryloxo ligands at 120 °C for 24 h (Table 6). Surprisingly, by employing ligand **1**, an excellent yield (99%) of the corresponding imine and a high *anti*-Markovnikov selectivity (*anti*-M:M = 94:6) was obtained. However, in the presence of **5** or **6** only low yields of imine

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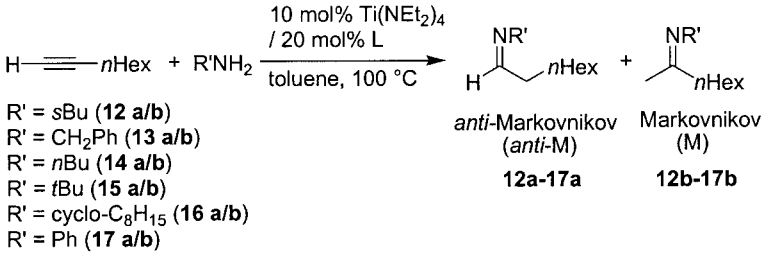
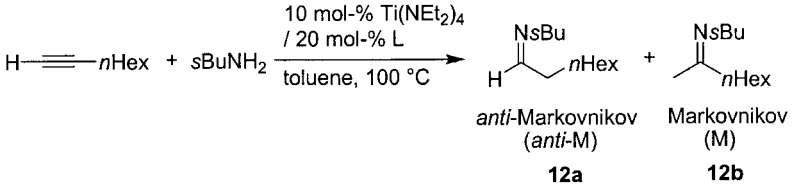
Table 4. Intermolecular hydroamination of 1-octyne with different amines using $Ti(NEt_2)_4$ and ligand **1** in comparison with $[Ti(NMe_2)_2$-$(2,6\text{-}tBu_2\text{-}4\text{-}Me\text{-}C_6H_2O)_2]$ (**24**) as catalyst.[a]



Entry	Ligand or Complex (**24**)	Amine	Conversion [%]	Yield[b] [%]	*anti*-M:M ratio[c]
1	**24**	benzylamine	100	99 (65)	25:75 (24:76)
2	**1**	benzylamine	100	99	20:80
3	**24**	*n*-butylamine	100	97 (58)	28:72 (28:72)
4	**1**	*n*-butylamine	100	99	25:75
5	**24**	*sec*-butylamine	100	98 (71)	8:92 (16:84)
6	**1**	*sec*-butylamine	100	98	10:90
7	**24**	cyclooctylamine	100	99 (82)	16:84 (22:78)
8	**1**	cyclooctylamine	100	99	14:86
9	**24**	*tert*-butylamine	n.r.	–	–
10	**1**	*tert*-butylamine	50	50	74:26
11[d]	**1**	*tert*-butylamine	75	58	88:12
12	**24**	aniline	100	99	4:96
13	**1**	aniline	100	99	22:78
14[d]	**1**	aniline	100	96	20:80

[a] Reaction conditions: 1.5 mmol 1-octyne, 1.8 mmol amine, 10 mol-% catalyst, Ti/L = 1:2, 2 mL toluene, 100 °C, 24 h, reaction conditions not optimized. [b] Yield is determined by GC analysis with dodecane or hexadecane as internal standard, isolated yield is given in parenthesis. [c] GC analysis was used to determine regioisomers, the ratio of regiomers of the isolated product after distillation is given in parenthesis. [d] Ti:L = 1:1.

Table 5. Hydroamination of 1-octyne with *sec*-butylamine in the presence of $Ti(NEt_2)_4$ and monodentate ligands using different Ti:L ratios.[a]



Entry	Ligand	Ti:L	Conversion [%]	Yield[b] [%]	*anti*-M:M ratio[c]
1	**1**	1:1	100	98	23:77
2	**1**	1:2	100	98	10:90
3	**1**	1:4	100	99	8:92
4	**5**	1:1	100	94	66:34
5	**5**	1:2	100	97	49:51
6	**5**	1:3	n.r.	–	–
7[d]	**5**	1:3	n.r.	–	–
8	**7**	1:1	100	88	87:13
9	**7**	1:2	100	94	94:6
10	**7**	1:3	n.r.	-	-
11	**8**	1:1	100	94	87:13
12	**8**	1:2	100	97	94:6
13	**8**	1:3	65	63	96:4
14	**8**	1:4	n.r.	–	–

[a] Reaction conditions: 1.5 mmol 1-octyne, 1.8 mmol amine, 10 mol-% catalyst, 2 mL toluene, 100 °C, 24 h. [b] Yield is determined by GC analysis with dodecane or hexadecane as internal standard. [c] GC analysis was used to determine the regioisomers. [d] Reaction with complex $[Ti(NMe_2)(2,6\text{-}Ph_2\text{-}C_6H_3O)_3]$ (**25**).

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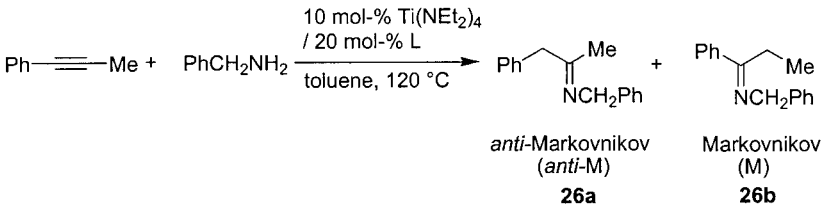
Table 6. Hydroamination of methylphenylacetylene with benzylamine using $Ti(NEt_2)_4$ and different monodentate ligands.[a]



Entry	Ligand	Conversion [%]	Yield[b] [%]	*anti*-M:M ratio[c]
1	**1**	100	99 (42)	94:6 (91:9)
2	**5**	24	24	74:26
3	**6**	42	16	65:35
4	**8**	100	51	88:12

[a] Reaction conditions: 1.5 mmol 1-octyne, 1.8 mmol amine, 10 mol-% catalyst, Ti/L = 1:2, 2 mL toluene, 120 °C, 24 h. [b] Yield is determined by GC analysis with dodecane or hexadecane as internal standard, isolated yield is given in parenthesis. [c] GC analysis was used to determine the regioisomers, the ratio of regiomers of the isolated product after distillation is given in parenthesis.

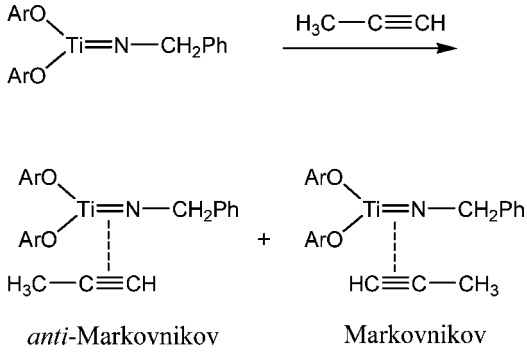
and low regioselectivity were observed (Table 6, Entries 2–3). In the presence of **8** the reaction gave 100% conversion but only 51% yield of the corresponding imine and moderate regioselectivity (Table 6, Entry 4).

Calculations on the Aryloxotitanium-Catalyzed Hydroamination of Terminal Alkynes

As discussed above, the hydroamination of terminal alkynes catalyzed by aryloxotitanium complexes shows high regioselectivity, which depends significantly on the changes of the substituent at the benzene ring of the aryloxo ligands. For example, hydroamination of alkynes with benzylamine shows regioselectivity in favor of the Markovnikov product by using 2,6-di-*tert*-butyl-4-methylphenol ligand **1**, while the *anti*-Markovnikov product is obtained by using 2,6-diisopropylphenol ligand **8**. Both ligands differ only in the substitution at the 2,6-positions. However, does this comparably small difference determine the regioselectivity?

Recently, we studied the combined experimental and theoretical investigation in the regioselectivite hydroamination of terminal alkynes by using (η^5-C_5H_5)-Ti(=NR)(NHR) as the active catalyst.[8a] We have found that this reaction is highly regioselective, i.e. substituted anilines favor Markovnikov products and *tert*-butylamine favors the *anti*-Markovnikov product. The regioselectivity is determined by the electrostatic attractive and steric repulsive effects in the preformed π complexes. Neither the kinetic nor thermodynamic parameters occurring during the formation of the [2+2]-cycloaddition step determine the regioselectivity.

In our model calculations, we have used propyne as the terminal alkyne, and benzylamine as the amine, and the aryloxo ligand (ArO) is modeled by 2,6-diisopropyl-phenoxo **8′** and 2,6-di-*tert*-butyl-phenoxo ligands **1′**. On the basis of the experimental findings, the active catalyst has been considered to be the bis-aryloxotitaniumimido complex, $(ArO)_2Ti(=N–CH_2Ph)$, which coordinates with the attacking propyne to form the π complexes in both Markovnikov and *anti*-Markovnikov ways, as shown in Scheme 4. Both complexes should be in equilibrium during their formation, and their equilibrium constant (K) is determined by their relative Gibbs free energy ($\Delta G = -RT\ln K$), which is also the difference between the two competing reaction energies on the basis of the active catalyst $(ArO)_2Ti(=N–CH_2Ph)$ and propyne. The consequence of this is that the more stable π complex should be higher in concentration and should also lead to the more dominant product. Since it was not possible to perform the corresponding frequency calculation, it was also not possible to obtain the thermal correction for the Gibbs free energy, therefore, the calculated relative energies (ΔH) are taken as approximate Gibbs free energies (ΔG) to determine the equilibrium constant and ratio of *anti*-Markovnikov and Markovnikov π complexes. The working temperature used in the experiment is 373 K. The optimized structures are shown in Figure 1 and Figure 2, and the calculated energies are given in Table 7. Selected structural parameters are given in the Table 8 and Table 9.



Scheme 4. *anti*-Markovnikov and Markovnikov coordination of propyne.

For the reaction with 2,6-diisopropylphenoxo **8′** as the ligand, both the *anti*-Markovnikov π complex (**AM-1**) and the Markovnikov one (**M-1**) have been optimized at the B3LYP level of theory with the LANL2DZ and LANL2DZ(d) basis sets. The optimized structures are shown in Figure 1. At B3LYP/LANL2DZ(d), the former is

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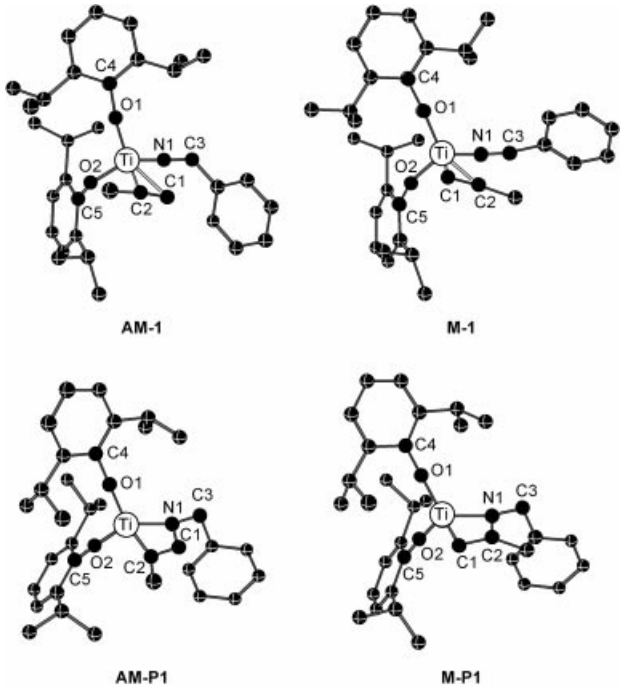

Figure 1. Optimized structures for the π complexes and the cycloaddition products with 2,6-diisopropylphenoxo ligand **8′** (hydrogen atoms are omitted for clarity).

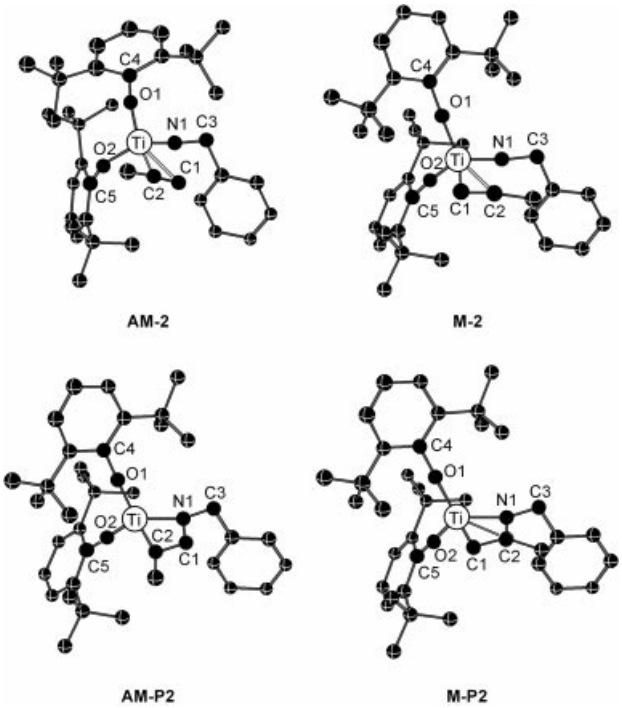

Figure 2. Optimized structures for the π complexes and the cycloaddition products with 2,6-di-*tert*-butylphenoxo ligand **1′** (hydrogen atoms are omitted for clarity).

computed to be lower in energy than the latter by 1.25 kcal/mol, and, therefore, **AM-1** should be more dominant over **M-1**. This should also be the case for subsequent products. This energy difference gives a percentage ratio of 84 to 16 for *anti*-Markovnikov to Markovnikov products, and this ratio matches the experimental finding (86:14) perfectly. Both [2+2]-cycloaddition products (**AM-P1** and **M-P1**) are close in energy (0.76 kcal/mol) at B3LYP/LANL2DZ(d).

In contrast to 2,6-di-*tert*-butyl-phenoxo **1′** as ligand, it is only possible to get the π complexes optimized at B3LYP/LANL2DZ, and further optimization at B3LYP/LANL(d)

Table 7. Computed total (E_{tot}, au) and relative energies (ΔH, kcal/mol) of the π complexes and [2+2]-cycloaddition products.

Isomers	E_{tot} (B3LYP/LANL2DZ)	E_{tot} [B3LYP/LANL2DZ(d)]	ΔH
AM-1	–1585.92067	–1586.24169	0.00
M-1	–1585.91997	–1586.23997	1.25
AM-P1	–1585.94721	–1586.27616	0.00
M-P1	–1585.94292	–1586.27737	–0.76
AM-2	–1743.09715	[–1743.45068][a]	[0.00][a]
M-2	–1743.10942	[–1743.46108][a]	[–6.35][a]
AM-P2	–1743.14414	–1743.50695	0.00
M-P2	–1743.14566	–1743.50798	–0.65

[a] Single-point energies at B3LYP/LANL2DZp//B3LYP/LANL2DZ.

Table 8. B3LYP/LANL2DZp optimized structures (in Å and °) for the π complexes and the cycloaddition products with 2,6-diisopropylphenoxo ligands.[a]

	AM-1	**AM-P1**	**M-1**	**M-P1**
Ti–C1	2.429 [2.490]	2.197 [2.250]	2.317 [2.328]	1.941 [1.969]
Ti–C2	2.370 [2.415]	1.963 [1.991]	2.545 [2.630]	2.241 [2.296]
Ti–C1/C2	4.799 [4.905]	4.160 [4.241]	4.862 [4.958]	4.182 [4.265]
Ti–N1	1.701 [1.706]	1.882 [1.888]	1.706 [1.711]	1.896 [1.901]
Ti–O1	1.838 [1.834]	1.811 [1.809]	1.837 [1.833]	1.810 [1.808]
Ti–O2	1.841 [1.836]	1.806 [1.804]	1.832 [1.828]	1.804 [1.804]
Ti–N1–C3	178.0 [177.5]	158.3 [155.7]	170.1 [170.2]	152.6 [150.6]
Ti–O1–C4	167.3 [171.0]	178.5 [176.6]	169.2 [171.5]	175.2 [175.7]
Ti–O1–C5	146.6 [156.4]	170.2 [176.2]	153.1 [159.4]	176.3 [178.5]
N1–Ti–C1–C2	176.6 [175.1]	179.5 [179.6]	–6.9 [–6.3]	0.1 [0.1]

[a] B3LYP/LANL2DZ values are given in square brackets.

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Table 9. B3LYP/LANL2DZp optimized structures (in Å and °) for the π complexes and the cycloaddition products with 2,6-di-*tert*-butylphenoxo ligands.[a]

	AM-2	AM-P2	M-2	M-P2
Ti–C1	[2.536]	2.204 [2.257]	[2.231]	1.940 [1.965]
Ti–C2	[2.542]	1.963 [1.991]	[2.530]	2.252 [2.307]
Ti–C1/C2	[5.078]	4.167 [4.248]	[4.761]	4.192 [4.272]
Ti–N1	[1.697]	1.888 [1.891]	[1.720]	1.904 [1.909]
Ti–O1	[1.864]	1.818 [1.816]	[1.845]	1.817 [1.814]
Ti–O2	[1.858]	1.821 [1.818]	[1.840]	1.820 [1.817]
Ti–N1–C3	[174.9]	157.9 [155.4]	[173.3]	152.8 [150.7]
Ti–O1–C4	[163.9]	178.3 [178.2]	[174.9]	179.6 [179.3]
Ti–O1–C5	[150.5]	175.6 [175.7]	[171.6]	176.4 [178.3]
N1–Ti–C1–C2	[167.4]	–178.8 [–178.8]	[4.5]	1.9 [1.7]

[a] B3LYP/LANL2DZ values are given in square brackets.

leads directly to the [2+2]-product, indicating the rather low activation barrier for the cycloaddition step. In order to make comparisons, single-point energy calculations at the B3LYP/LANL2DZ(d) level with the B3LYP/LANL2DZ optimized geometries have been carried out. The optimized structures are shown in Figure 2. The computed energy differences indicate that the *anti*-Markovnikov π complex (**AM-2**) is computed to be higher in energy than the Markovnikov one (**M-2**) by 6.53 kcal/mol, and this energy difference completely favors the Markovnikov product over the *anti*-Markovnikov product (>99%). However, this calculated result agrees only qualitatively with the experimental finding of the same trend, and quantitatively overestimated the regioselectivity, since the observed regioselectivity is 80 to 20. As expected, both cycloaddition products (**AM-P2** and **M-P2**) are close in energy (0.65 kcal/mol).

Apart from the agreement between theory and experiment, it is interesting to understand the driving force for the regioselectivity. Since both aryloxo ligands differ only in the substituents in the 2,6-positions, e.g. *tert*-butyl and isopropyl, it is expected that their regioselectivity should be directly related with the steric effect of these substitutes.

From a structural point of view, there are many possible explanations for the reduction in strain energy caused by the steric effect, (a) the C–O–Ti angles of the aryloxo ligands, (b) the Ti–N–C angle of the imido ligand, (c) the bulky substituents at 2,6-positions of the aryloxo ligands, (d) the interaction between the propyne methyl group and the phenyl group of imido ligands in the Markovnikov π complexes, and (e) the interaction between the propyne methyl group and the *tert*-butyl or isopropyl groups of the aryloxo ligands. All these factors work together, and their net effect is reflected by the distances of Ti to the alkyne triple bond or sum of the two Ti–C distances, i.e.; the shorter the distances, the stronger the interaction, and the more stable the π complex.

On this basis, it is clearly seen that the more stable *anti*-Markovnikov π complex (**AM-1**) of the isopropyl-substituted aryloxo ligand has a shorter Ti–C distance than the less stable Markovnikov isomer (**M-1**) (4.905 vs. 4.958 Å, Table 8). For the *tert*-butyl-substituted aryloxo ligand, the Ti–C distance of the more stable Markovnikov π complex (**M-2**) is shorter than that of the less stable *anti*-Markovnikov isomer (**AM-2**) (4.761 vs. 5.078 Å, Table 9). Thus, the Ti–C distance correlates nicely with the relative stability of these π complexes. This clearly shows that the observed regioselectivity is determined by the steric difference between *tert*-butyl and isopropyl substituents at the 2,6-position of the aryloxo ligand.

In summary, we presented a detailed study on the titanium-catalyzed hydroamination of terminal alkynes in the presence of 17 different alkoxo and aryloxo ligands. By using the "right" ligand all the reactions shown can be performed in good to excellent yield and with high regioselectivity. Interestingly, by slight variations of the sterics of the aryloxo ligands the selectivity can be controlled and a selectivity switch can even be obtained. Such a control of regioselectivity is still rare for addition processes to unsaturated compounds. Computational studies demonstrate that the observed change of regioselectivity is determined by steric factors.

Experimental Section

General Remarks: All reactions were carried out under argon. Chemicals were obtained from Aldrich, Fluka, Acros and Strem and unless otherwise noted were used without further purification. Amines were distilled from CaH_2. Alkynes were degassed, flushed with argon and stored over molecular sieves (4 Å). Absolute solvents were purchased from Fluka. All operations were carried out under an argon atmosphere. All compounds were characterized by ^{1}H NMR, ^{13}C NMR, MS and IR spectroscopy. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker ARX 400 spectrometer. The ^{1}H and ^{13}C NMR chemical shifts are reported relative to the center of solvent peak [$CDCl_3$: 7.25 (^{1}H), 77.0 (^{13}C); [D_8]THF: 1.73 (^{1}H), 25.2 (^{13}C)]. EI mass spectra were recorded with an AMD 402 spectrometer (70 eV, AMD Intectra GmbH). IR spectra were recorded with a Nicolet Magna 550. Elemental analyses were determined by C/H/N/S-Analysator 932 (Leco). GC analysis was performed with a Hewlett Packard HP 6890 chromatograph with a 30 m HP5 column. All yields reported in Tables 1–6 refer to GC yields using dodecane or hexadecane as an internal standard. We have described the imine *N*-*tert*-butyl-octylidene-amine (**15a**) previously.[8c] The titanium catalysts bis(2,6-di-*tert*-butyl-4-methylphenoxo)bis(dimethylamido)titanium ([$Ti(NMe_2)_2$(2,6-tBu_2-4-Me-$C_6H_2O)_2$]) (**24**)[11b] and bis(2,6-di-phenylphenoxo)titanium dichloride ([$TiCl_2$(2,6-Ph_2-$C_6H_3O)_2$])[13] were prepared following literature procedures.

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Tris(2,6-diphenylphenoxo)(dimethylamido)titanium ([Ti(NMe$_2$)(2,6-Ph$_2$-C$_6$H$_3$O)$_3$]) (25): 2,6-Diphenylphenol (3.50 g, 14.1 mmol) was added to tetrakis(dimethylamido)titanium (1.05 g, 4.7 mmol) in toluene (75 mL). While stirring at room temperature for 2 days orange microcrystals precipitated. The resulting orange precipitate was collected by filtration, washed with toluene (10 mL), and dried under vacuum. M.p. 112–117 °C (dec.); yield: 1.91 g (49%). ^{1}H NMR ([D$_8$]THF, 400 MHz): δ = 6.95–7.20 (m, 39 H), 1.38 (s, 6 H) ppm. ^{13}C NMR ([D$_8$]THF, 100 MHz): δ = 159.8, 140.4, 133.4, 130.7, 130.2, 128.7, 127.3, 121.8, 45.6 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 827 (21) [M$^+$], 583 (57), 582 (100), 538 (71), 537 (95), 293 (24), 291 (16), 246 (49), 245 (17). FT IR (nujol): 3050, 3024, 2777, 1598, 1494, 1408, 1234, 905, 756, 720, 700 cm^{-1}. $C_{56}H_{45}NO_3Ti$ (827.83): calcd. C 81.25, H 5.48, N 1.69; found C 80.72, H 5.30, N 1.66.

General Procedure for Hydroamination Reactions: In an Ace-pressure tube under an argon atmosphere the ligand (2,6-diisopropylphenol, 2,6-di-*sec*-butylphenol or 2,6-di-*tert*-butyl-4-methylphenol) (2.2 mmol) was dissolved in 7.5 mL toluene. Amine (13.5 mmol), 1-octyne (11.3 mmol) and Ti(NEt$_2$)$_4$ (1.1 mmol) were added to this solution. When preparing the Markovnikov isomers as the main product, complex [Ti(NMe$_2$)$_2$(2,6-*t*Bu$_2$-4-Me-C$_6$H$_2$O)$_2$] (1.1 mmol) was used and dissolved in 7.5 mL toluene. The pressure tube was fitted with a Teflon cap and heated at 100 °C for 24 h in an oil bath. Afterwards all volatiles were removed and the product was isolated by fractional distillation in vacuo. The imine products were isolated as a mixture of *anti*-Markovnikov and Markovnikov products. The ratio of the regioisomers was determined by GC analysis. After isolation (via distillation) this ratio might differ because of the different boiling points of the regioisomers (see Tables 1, 2, 4, and 6). The Markovnikov product is a mixture of the *E*- and *Z*-isomers; thus, some NMR resonances were present as two signals (indicated below by "+"), representing both isomers.

***N*-(*sec*-Butyl)octylideneamine/*N*-(*sec*-Butyl)-2-octylidene-2-amine (ratio 96:4) (12a/12b):** 2,6-Di-*sec*-butylphenol was used as the ligand. Colorless oil; b.p. 41–43 °C/0.1 mbar; 70% (1.47 g) isolated yield (98% GC yield). Data for *anti*-Markovnikov product (**12a**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 7.57 (t, *J* = 5.2, 1 H), 2.88 (sext, *J* = 6.5 Hz, 1 H), 2.20 (m, 2 H), 1.46 (quin, *J* = 7.5 Hz, 4 H), 1.17–1.35 (m, 8 H), 1.11 (d, *J* = 6.3 Hz, 3 H), 0.85 (m, 3 H), 0.76 (t, *J* = 7.5 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 162.9, 67.9, 35.7, 31.7, 30.4, 29.2, 29.0, 26.4, 22.6, 22.4, 14.0, 11.0 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 183 (1) [M$^+$], 182 (2), 154 (38), 112 (24), 99 (100), 84 (44), 71(15), 70 (37), 69 (30), 57 (50), 56 (44), 55 (33), 44 (52), 43 (29), 42 (27), 41 (75), 29 (47), 28 (40), 27 (32). FT IR (neat): 1669 (C=N) cm^{-1}. HRMS: Calcd. for $C_{12}H_{25}N$: 183.19870; found 183.19762.

***N*-(*sec*-Butyl)-2-octylidene-2-amine/*N*-(*sec*-Butyl)octylideneamine (ratio 84:16) (12b/12a):** Complex [Ti(NMe$_2$)$_2$(2,6-*t*Bu$_2$-4-Me-C$_6$H$_2$O)$_2$] was used. Colorless oil; b.p. 49–50 °C/0.1 mbar; 71% (1.49 g) isolated yield (98% GC yield). Data for Markovnikov product (**12b**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 3.34 + 3.28 (sext, *J* = 6.5 Hz, 1 H), 2.13–2.24 (m, 2 H), 1.94 + 1.77 (s, 3 H), 1.39–1.52 (m, 4 H), 1.21–1.33 (m, 6 H), 1.02 + 1.03 (d, *J* = 6.3 Hz, 3 H), 0.82–0.89 (m, 3 H), 0.73–0.81 (m, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 167.8 + 167.4, 56.4 + 55.9, 43.1, 32.1 + 31.7, 31.0 + 30.9, 29.5 + 29.0, 27.1 + 26.9, 22.5, 21.7 + 21.2, 16.5, 14.0, 11.1 ppm. MS (EI) *m*/*z* (%): 183 (4) [M$^+$], 182 (6), 154 (48), 140 (20), 126 (40), 113 (88), 112 (21), 98 (100), 85 (39), 84 (66), 70 (32), 58 (31), 57 (26), 55 (14), 42 (59), 41 (31), 29 (15). FT IR (neat): 1661 (C=N) cm^{-1}.

***N*-Benzyloctylideneamine/*N*-benzyl-2-octylideneamine (ratio 87:13) (13a/13b):** 2,6-Diisopropylphenol was used as the ligand. Colorless oil; b.p. 97–98 °C/0.1 mbar; 41% (0.98 g) isolated yield (72% GC yield). Data for *anti*-Markovnikov product (**13a**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 7.78 (tt, *J* = 5.0, 1.4 Hz, 1 H), 7.23–7.33 (m, 5 H), 4.56 (s, 2 H), 2.27–2.35 (m, 2 H), 1.51–1.62 (m, 2 H), 1.21–1.39 (m, 8 H), 0.88 (m, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 166.4, 139.4, 128.4, 127.9, 126.8, 65.1, 36.0, 31.7, 29.2, 29.0, 26.0, 22.6, 14.0 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 217 (1) [M$^+$], 147 (23), 146 (19), 133 (52), 132 (23), 91 (100), 65 (16), 41 (14), 28 (25). FT IR (neat): 1668 (C=N) cm^{-1}. HRMS: Calcd. for $C_{15}H_{23}N$: 217.18304; found 217.18328.

***N*-Benzyl-2-octylideneamine/*N*-Benzyloctylideneamine (ratio 76:24) (13b/13a):** Complex [Ti(NMe$_2$)$_2$(2,6-*t*Bu$_2$-4-Me-C$_6$H$_2$O)$_2$] was used. Colorless oil; b.p. 98 °C/0.1 mbar; 65% (1.56 g) isolated yield (99% GC yield). Data for Markovnikov product (**13b**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 7.20–7.35 (m, 5 H), 4.51 + 4.48 (s, 2 H), 2.27–2.35 (m, 2 H), 2.07 + 1.89 (s, 3 H), 1.51–1.63 (m, 2 H), 1.31 (m, 6 H), 0.88 (m, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 171.8 + 171.4, 140.5, 128.3, 127.7 + 127.6, 126.4, 55.0 + 54.6, 42.9, 31.6 + 31.5, 29.4 + 29.1, 26.6 + 26.3, 22.5, 17.5, 14.0. MS (EI, 70 eV) *m*/*z* (rel. intensity): 217 (2) [M$^+$], 160 (15), 147 (88), 146 (57), 91 (100). FT IR (neat): 1663 (C=N) cm^{-1}.

***N*-Butyloctylideneamine/*N*-Butyl-2-octylidene-2-amine (ratio 91:9) (14a/14b):** 2,6-Di-*sec*-butylphenol was used as the ligand. Colorless oil; b.p. 57–58 °C/0.13 mbar; 50% (1.05 g) isolated yield (88% GC yield). Data for *anti*-Markovnikov product (**14a**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 7.59 (tt, *J* = 5.0, 1.4 Hz, 1 H), 3.32 (dt, *J* = 7.1, 1.0 Hz, 2 H), 2.16–2.22 (m, 2 H), 1.44–1.58 (m, 4 H), 1.20–1.33 (m, 10 H), 0.88 (t, *J* = 7.3 Hz, 3 H), 0.84 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 164.8, 61.1, 35.8, 32.8, 31.7, 29.2, 29.0, 26.1, 22.6, 20.3, 14.0, 13.8 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 183 (0.7) [M$^+$], 182 (1), 140 (10), 112 (25), 99 (32), 84 (100), 70 (19), 57 (69), 56 (40), 55 (17), 43 (16), 42 (26), 41 (46), 29 (42). FT IR (neat): 1671 (C=N) cm^{-1}. HRMS: Calcd. for $C_{12}H_{25}N$: 183.19870: found 183.19790.

***N*-Butyl-2-octylidene-2-amine/*N*-butyloctylideneamine (ratio 72:28) (14b/14a):** Complex [Ti(NMe$_2$)$_2$(2,6-*t*Bu$_2$-4-Me-C$_6$H$_2$O)$_2$] was used. Colorless oil; b.p. 45–46 °C/0.1 mbar; 58% (1.22 g) isolated yield (97% GC yield). Data for Markovnikov product (**14b**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 3.15–3.25 (m, 2 H), 2.19 (m, 2 H), 1.95 + 1.76 (s, 3 H), 1.42–1.62 (m, 4 H), 1.20–1.39 (m, 8 H), 0.81–0.95 (m, 6 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 170.3 + 169.8, 51.1 + 50.5, 42.9, 33.3 + 33.0, 32.1 + 31.6, 29.4 + 29.1, 27.0 + 26.7, 22.5, 20.7, 16.8, 13.99, 13.96 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 183 (2) [M$^+$], 182 (3), 140 (21), 126 (43), 113 (41), 98 (100), 84 (23), 71 (80), 70 (16), 57 (22), 56 (21), 55 (10), 42 (36), 41 (23), 29 (12). FT IR (neat): 1662 (C=N) cm^{-1}.

***N*-Cyclooctyloctylideneamine/*N*-Cyclooctyl-2-octylidene-2-amine (ratio 96:4) (16a/16b):** 2,6-Diisopropylphenol was used as the ligand. Colorless oil; b.p. 95 °C/0.14 mbar; 65% (1.76 g) isolated yield (94% GC yield). Data for *anti*-Markovnikov product (**16a**): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 7.55 (t, *J* = 5.4 Hz, 1 H), 3.07 (m, 1 H), 2.16 (m, 2 H), 1.65–1.77 (m, 4 H), 1.41–1.58 (m, 12 H), 1.20–1.32 (m, 8 H), 0.85 (m, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 161.5, 71.3, 35.7, 34.2, 31.7, 29.1, 29.0, 27.2, 26.3, 25.6, 24.1, 22.6, 14.0 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 237 (3) [M$^+$], 236 (2), 194 (14), 166 (32), 153 (42), 152 (37), 138 (95), 128 (23), 124 (17), 110 (37), 96 (23), 82 (50), 69 (78), 67 (30), 56 (44), 55 (68), 44 (56), 43 (57), 42 (19), 41 (100), 29 (43). FT IR (neat): 1668 (C=N) cm^{-1}. HRMS: Calcd. for $C_{16}H_{31}N$: 237.24565: found 237.24508.

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***N*-Cyclooctyl-2-octylidene-2-amine/*N*-Cyclooctyloctylideneamine (ratio 78:22) (16b/16a):** Complex [Ti(NMe_2)$_2$(2,6-*t*Bu_2-4-Me-C_6H_2O)$_2$] was used. Colorless oil; b.p. 88 °C/0.1 mbar; 82% (2.21 g) isolated yield (99% GC yield). Data for Markovnikov product (**16b**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.37–3.52 (m, 1 H), 2.12–2.21 (m, 2 H), 1.91 + 1.77 (s, 3 H), 1.60–1.76 (m, 2 H), 1.41–1.59 (m, 12 H), 1.20–1.36 (m, 8 H), 0.81–0.93 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.9 + 165.6, 59.9 + 59.3, 43.0, 34.3 + 34.0, 31.7 + 31.6, 29.2 + 29.0, 27.1, 26.9 + 26.8, 26.0 + 25.9, 24.5, 22.5, 16.4, 14.0 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 237 (10) [M^+], 222 (16), 194 (25), 180 (91), 167 (48), 166 (42), 154 (24), 152 (100), 128 (68), 124 (18), 110 (23), 96 (22), 82 (27), 70 (21), 69 (53), 58 (34), 55 (37), 41 (36). FT IR (neat): 1659 (C=N) cm^{-1}.

***N*-(2-Octylidene)aniline/*N*-(Octylidene)aniline (ratio 70:30) (17b/17a):** 2,6-Diisopropylphenol was used as the ligand. Colorless oil; b.p. 79–80 °C/0.12 mbar; 37% (0.85 g) isolated yield (86% GC yield). Data for Markovnikov product (**17b**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.24–7.30 (m, 2 H), 6.98–7.04 (m, 1 H), 6.65–6.70 (m, 2 H), 2.37–2.42 + 2.08–2.13 (m, 2 H), 2.14 + 1.76 (s, 3 H), 1.60–1.70 + 1.42–1.50 (m, 2 H), 1.14–1.42 (m, 6 H), 0.83–0.90 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.7 + 172.2, 151.6 + 151.1, 128.8 + 128.7, 122.9 + 122.8, 119.5, 41.7 + 34.0, 31.7 + 31.4, 29.1 + 29.0, 26.8 + 26.3, 22.6 + 22.4, 19.4, 14.0 + 13.9 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 203 (14) [M^+], 188 (4), 146 (30), 133 (93), 132 (93), 119 (41), 118 (69), 93 (31), 92 (29), 77 (100), 51 (31), 43 (22), 42 (25), 41 (30), 39 (22), 29 (27), 28 (20), 27 (25). FT IR (neat): 1662 (C=N) cm^{-1}. HRMS: Calcd. for $C_{14}H_{21}N$: 203.16740; found 203.16682.

***N*-Benzyl-(1-methyl-2-phenylethylidene)amine/*N*-Benzyl(1-phenylpropylidene)amine (ratio = 91:9) (26a/26b):** 2,6-Di-*tert*-butyl-4-methylphenol was used as the ligand. Colorless oil; b.p. 104 °C/0.13 mbar; 42% (1.05 g) isolated yield (99% GC yield). Data for *anti*-Markovnikov product (**26a**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.12–7.25 (m, 10 H), 4.41 (s, 2 H), 3.55 (s, 2 H), 1.73 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 169.7, 140.3, 137.5, 129.1, 128.5, 128.4, 127.7, 126.5, 55.4, 49.7, 17.0 ppm. MS (EI, 70 eV) *m*/*z* (rel. intensity): 223 (6) [M^+], 132 (21), 91 (100), 65 (16). FT IR (neat): 1658 (C=N) cm^{-1}. HRMS: Calcd. for $C_{16}H_{17}N$: 223.13609; found 223.13533.

Computational Details: In order to understand the origin of the observed regioselectivity by employing aryloxotitanium complexes in the hydroamination of terminal alkynes, density functional theory[14] calculations have been performed. All structures have been optimized at the B3LYP density functional level of theory in combination with the LANL2DZ basis set, further calculations have been done with the extended L2NL2DZ basis set including a set of polarization functions [LANL2DZ(d)].[15] Due to the large size and low symmetry, it has not been possible to carry out the frequency calculation for characterizing the optimized structures as energy minimum structures. However, all optimized structures are considered to be energy minima since they all have positive eigenvalues from the Hessian calculations.[16] All calculations have been done with the Gaussian 98 program.[17]

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