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Fabien Grasset, Richard Welter, Pierre Braunstein, Hélène Olivier-Bourbigou, Lionel Magna. Titanium Complexes with Functional Alkoxido Ligands for Selective Ethylene Dimerization – A High Throughput Experimentation Approach. ChemCatChem, 2021, 13 (9), pp.2167-2178. 10.1002/cctc.202002029 . hal-03248781

**HAL Id: hal-03248781**

**<https://ifp.hal.science/hal-03248781>**

Submitted on 3 Jun 2021

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# Titanium Complexes with Functional Alkoxido Ligands for Selective Ethylene Dimerization – A High Throughput Experimentation Approach

Fabien L. Grasset,<sup>[a]</sup> Richard Welter,<sup>[b]</sup> Pierre Braunstein,<sup>\*,[c]</sup> H            ,<sup>[a]</sup> and Lionel Magna<sup>\*,[a]</sup>

*Dedicated to Prof. Dr. Maurizio Peruzzini on the occasion of his 65th birthday, with our warmest congratulations.*

New titanium complexes of general formula  $[\text{Ti}(\text{OR})_2(\text{OiPr})_2]$ , containing functionalized alkoxido ligands, were developed for the selective catalytic dimerization of ethylene to 1-butene using a combined High Throughput Screening (HTS) / Design of Experiment (DoE) approach. First, a library of 19 ligands was elaborated and a primary screening spotted the phosphorus-functionalized alkoxido ligands as most promising. A second, more focused library containing 8 alkoxidophosphane ligands was then developed. A longer linear spacer between the

alkoxido and the phosphorus functions, as in  $[\text{Ti}(\mathbf{19})_2(\text{OiPr})_2]$ , was found beneficial for this catalytic reaction. After identification of the best co-catalyst ( $\text{AlEt}_3$ ) and co-ligand ( $\text{OnBu}$ ), final optimization of the reaction conditions was performed using a design of experiments (DoE) approach. The complex  $[\text{Ti}(\mathbf{19})_2(\text{OnBu})_2]$  was shown to selectively dimerize ethylene in 1-butene ( $C_4(\alpha) = 93\%$  ( $99\pm\%$ )) at 30 bar  $\text{C}_2\text{H}_4$  and  $55^\circ\text{C}$  with  $\text{AlEt}_3$  as co-catalyst, giving very high activity and selectivity for a molecular titanium catalyst ( $13000\text{ g g}_{\text{T}}^{-1}\text{ h}^{-1}$ , 93% 1-butene).

## 1. Introduction

The design of new homogeneous organometallic catalysts leading to high conversion and selectivity is based on finding adequate ligand/metal combinations under suitable experimental conditions. Since it is well known in molecular chemistry that even small modifications in the ligand structure can significantly impact the catalytic properties, although their extent remains very difficult to predict, a systematic exploration of the whole metal-ligand space for a given reaction is a


challenging task. A strategy that has emerged to accelerate this catalyst development is based on the evaluation of structurally diverse and meaningful ligand libraries through High-Throughput Screening techniques (HTS).<sup>[1]</sup> This strategy allows the chemist to switch from a “make one, screen one” approach to a rapid and parallel screening of libraries of compounds. This approach has been remarkably efficient in the field of olefin polymerization catalysis, for which the screening of ligand libraries has enabled the fine-tuning of the physical properties of polyolefinic materials.<sup>[2]</sup>


The closely related ethylene oligomerization (di-, tri- or tetramerization) reaction, which is the focus of the present study, continues to represent a research area of considerable academic and industrial interest and numerous reviews have examined the catalytic performances of diverse systems resulting from pre-catalysts from groups 4–10 metals.<sup>[3]</sup> In particular, titanium-based systems are widely known for selectively dimerizing ethylene to 1-butene,<sup>[4]</sup> even if recent work has demonstrated their potential for the selective production of 1-hexene.<sup>[5]</sup> In particular, it has been known since the 1960s that tetraalkoxido titanium complexes, upon activation by triethylaluminum ( $\text{AlEt}_3$ ), allow the conversion of ethylene in 1-butene.<sup>[6]</sup> The system has been improved over the years and was further developed into the commercial AlphabutoI® process.<sup>[7]</sup> Attempts to optimize the activity and the selectivity of the reaction have been essentially conducted by introducing external modifiers based on oxygen-, nitrogen-, or phosphorous-donors Lewis bases.<sup>[8]</sup> With the aims to better control and fine-tune the metal coordination sphere towards improved catalytic properties, we recently developed a promising family of titanium complexes where the modifier was incorporated in the aryloxido ligands,<sup>[9]</sup> that we extend now to alkoxido ligands. Potentially chelating ligands limit the structural diversity and sometimes difficult to

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 Supporting information for this article is available on the WWW under <https://doi.org/10.1002/cctc.202002029> Supporting Information contains experimental details, CCDC reference numbers 2038911-2038913 and 2044622. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

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control ligand rearrangements encountered in metal complexes with monodentate alkoxides.<sup>[10]</sup> We report herein a three-steps HTS-1/HTS-2/DoE (HTS=High Throughput Screening, DoE=Design of Experiment) combined approach towards heteroatom-functionalized alkoxido titanium complexes for the selective dimerization of ethylene. The two first steps consisted in the generation and HTS of libraries of functionalized alkoxido titanium complexes while optimization of the best catalyst was carried out in the third step using DoE.

## 2. Results and Discussion

### 2.1. Generation of a Library of Alkoxido Ligands Precursors

Owing to their major impact on catalysis, both the electronic and steric properties of the ligand should be systematically explored. Using various alcohols as precursors to the functionalized alkoxido ligands, the first variable we examined was the functionalization **Z** (Figure 1). Aromatic, oxygen-, nitrogen-, sulfur- and phosphorus-functionalized alcohols were thus considered. Furthermore, the length of the "spacer", i.e. the carbon chain between the OH group and **Z**, was chosen to correspond to 2 or 3 carbon atoms in order to allow the

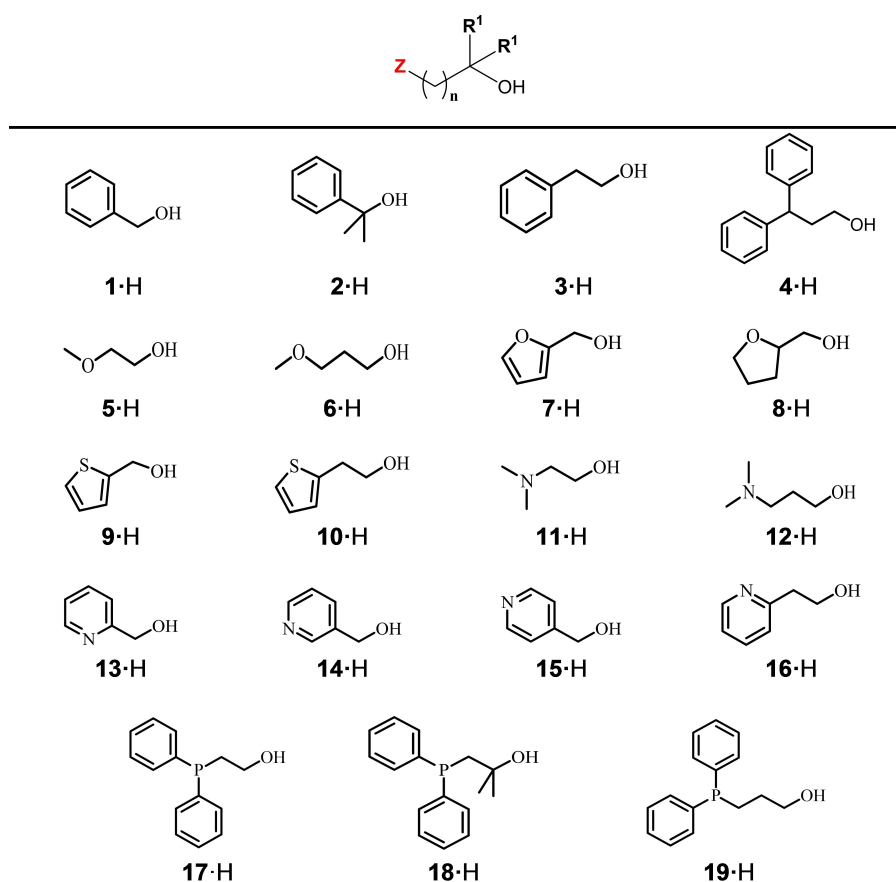
formation of 5- or 6-membered chelates, respectively, in case the donor atom of **Z** would coordinate to titanium. Finally, the influence of the steric hindrance around the oxygen donor was examined as a function of the **R**<sup>1</sup> group (H or Me). These considerations led to select the ligand library shown in Figure 1.

All the compounds shown in Figure 1 are commercially available, except the three phosphorus ligands **17·H**–**19·H**. These were synthesized according to a general procedure<sup>[11,12]</sup> which involves the reaction of LiPPh<sub>2</sub> with the corresponding chloroalcohol (Scheme 1).

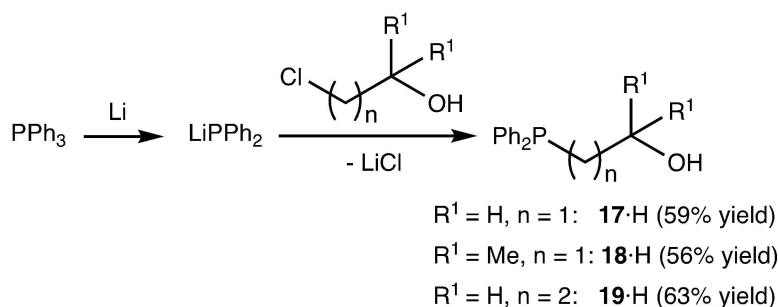
The desired products were obtained in moderate yields and were fully characterized by <sup>1</sup>H, <sup>13</sup>C and <sup>31</sup>P NMR spectroscopy (see ESI and Figure S1 for **19·H**). Single crystals were also obtained for **19·H** and their study by X-ray diffraction revealed that the alkyl chain, one phenyl group and the phosphorous atom are coplanar (Figure 2). The metrical data are unexceptional.

### 2.2. Library of Titanium Complexes [Ti(OR)<sub>2</sub>(O*i*Pr)<sub>2</sub>]

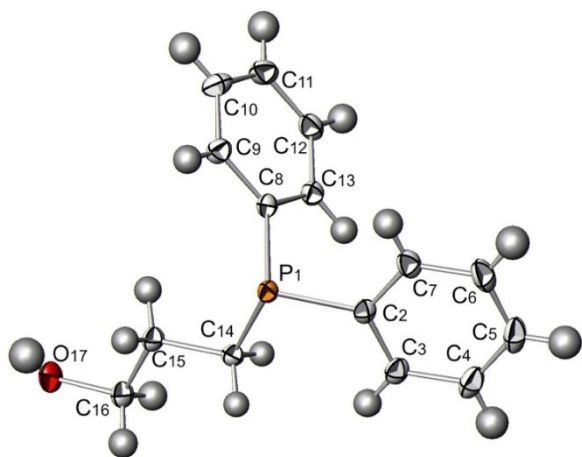
Considering the HTS approach pursued herein, we needed a protocol that would allow an easy, parallel synthesis of a library of complexes based on the ligand precursors shown in Figure 1.



**Figure 1.** Library of ligand precursors used for the first screening. In the following, a deprotonated alcohol **X·H** is referred to as ligand **X**.

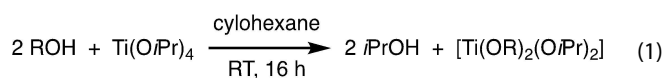


**Scheme 1.** Synthesis of the diphenylphosphino alcohols.



**Figure 2.** ORTEP view with full labelling scheme of **19**·H. Thermal ellipsoids include 50% of the electron density. The H atom on O17 is disordered over two positions with 50/50 occupancy; only one is represented. Main distances (Å) and angles (°): P<sub>1</sub>–C<sub>2</sub> 1.827(2), P<sub>1</sub>–C<sub>8</sub> 1.834(2), P<sub>1</sub>–C<sub>14</sub> 1.841(2), C<sub>16</sub>–O<sub>17</sub> 1.420(2); C<sub>2</sub>–P<sub>1</sub>–C<sub>8</sub> 99.8(1), C<sub>2</sub>–P<sub>1</sub>–C<sub>14</sub> 102.2(1), C<sub>8</sub>–P<sub>1</sub>–C<sub>14</sub> 100.7(1).

We reasoned that selective alcohol interchange could represent a potentially attractive and general access to di-substituted alkoxido titanium complexes, starting from cheap and commercially available [Ti(O*i*Pr)<sub>4</sub>] [Eq. (1)].<sup>[13,14,15]</sup>

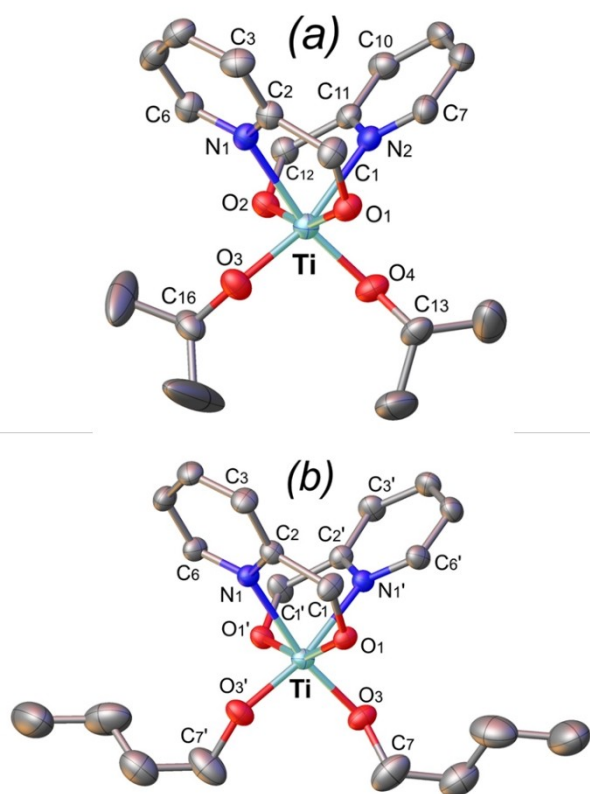


Di-substitution occurred with all the alcohols, affording complexes with the expected formulation [Ti(OR)<sub>2</sub>(O*i*Pr)<sub>2</sub>] based on <sup>1</sup>H NMR peaks integration. Most of them are viscous liquids. No purification of the complexes was required for the HTS approach described in this work. Most of the <sup>1</sup>H NMR spectra of the [Ti(OR)<sub>2</sub>(O*i*Pr)<sub>2</sub>] complexes presented broad signals for the H atoms in α position to the oxygen atoms and for the CH<sub>3</sub> protons of the isopropoxido ligands (see ESI, Figure S2a for [Ti(5)<sub>2</sub>(O*i*Pr)<sub>2</sub>]). This feature may indicate the presence of di- or polynuclear species with bridging ligands,<sup>[9]</sup> as encountered in (di-aldoximato)(di-isopropoxido)titanium complexes,<sup>[16]</sup> in mono (alkoxido-amino)titanium complexes,<sup>[17]</sup> and in [Ti(μ-OPh)(O-Ph)<sub>2</sub>(O*i*Pr)(OH*i*Pr)]<sub>2</sub>, a (di-isopropoxido)titanium complex with non-functionalized phenoxy ligands (see ESI). In the latter,

centrosymmetric complex, each Ti center is octahedrally coordinated by two bridging phenoxy ligands, one terminal phenoxy ligand trans to a μ-OPh and another cis to it, a O*i*Pr ligand and a *i*PrOH molecule trans to the terminal OPh ligand (see details in ESI, Figure S34 and Table S1). With more strongly coordinated ligands, such as **13**, the <sup>1</sup>H NMR spectrum presented sharp signals, including for the magnetically inequivalent OCH<sub>2</sub> atoms, consistent with a mononuclear complex (see ESI Figure S35 for [Ti(**13**)<sub>2</sub>(O*i*Pr)<sub>2</sub>]). The observation of a single peak for these hydrogen atoms at room temperature may indicate the occurrence of a dynamic process in solution for this molecule involving decoordination of the pyridine moiety, as observed in related systems.<sup>[14,17]</sup>

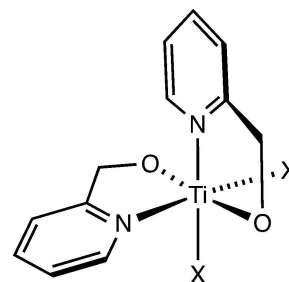
The mononuclear nature of [Ti(**13**)<sub>2</sub>(O*i*Pr)<sub>2</sub>] was confirmed by an X-ray diffraction analysis (Figure 3(a)), which is in agreement with literature data.<sup>[14,15]</sup> The structure of the titanium complex remained mononuclear when [Ti(OnBu)<sub>4</sub>] was used as precursor and the isopropoxido ligands were replaced by *n*-butoxido ligands (Figure 3(b)). ORTEP views with full labelling scheme of [Ti(**13**)<sub>2</sub>(O*i*Pr)<sub>2</sub>·1/2(C<sub>5</sub>H<sub>12</sub>)] and [Ti(**13**)<sub>2</sub>(OnBu)<sub>2</sub>] are provided in the ESI (Figures S35 and S36).

The structures of [Ti(**13**)<sub>2</sub>(O*i*Pr)<sub>2</sub>·1/2(C<sub>5</sub>H<sub>12</sub>)] (*a*) and [Ti(**13**)<sub>2</sub>(OnBu)<sub>2</sub>] belong to centrosymmetric space groups and both Δ-*cis* and Λ-*cis* enantiomers are therefore present in the unit cell. The octahedral environment around the Ti<sup>IV</sup> center is defined by the mutually trans alkoxido oxygen atoms O<sub>R</sub> and mutually cis nitrogen atoms of the chelates and the cis isopropoxido oxygen atoms O<sub>*i*Pr</sub> or *n*-butoxido oxygen atoms O<sub>*n*Bu</sub>, respectively. The only significant difference (3σ criterion) between these two structures is the larger Ti–O–C<sub>*n*Bu</sub> angle (Ti–O<sub>3</sub>–C<sub>7</sub> with 138.3(2)°) compared to Ti–O–C<sub>*i*Pr</sub> (Ti–O<sub>3</sub>–C<sub>16</sub> with 133.5(2)° and Ti–O<sub>4</sub>–C<sub>13</sub> with 132.5(2)°). However, these values are rather similar and their small difference could result from crystal packing effects and/or be of electronic origin, with a slightly larger participation of the oxygen lone pairs in the Ti–O bond involving the *n*-butoxido ligands. Note however that π-donation is likely to be weak in both complexes, a larger Ti–O–C angle being expected with increasing π-donation.<sup>[10]</sup> The metrical data for [Ti(**13**)<sub>2</sub>(OnBu)<sub>2</sub>] are very similar to those reported for [Ti(**13**)<sub>2</sub>(OtBu)<sub>2</sub>].<sup>[15]</sup> A search in the structural Cambridge data base concerning Ti<sup>IV</sup> complexes indicated 451 structures with Ti<sup>IV</sup> centers surrounded by 4 oxygen and 2 nitrogen atoms, forming an octahedral coordination sphere.



**Figure 3.** ORTEP views with partial labelling scheme of [Ti(13)<sub>2</sub>(OiPr)<sub>2</sub>]·1/2(C<sub>5</sub>H<sub>12</sub>) (a) and [Ti(13)<sub>2</sub>(OnBu)<sub>2</sub>] (b). Hydrogen atoms are omitted for clarity. Thermal ellipsoids include 50% of the electron density. Symmetry code for equivalent positions (′), corresponding to a C<sub>2</sub> axis passing through the Ti atom): 1-x, y, 1/2-z. Selected bond distances (Å) and angles (°) for [Ti(13)<sub>2</sub>(OiPr)<sub>2</sub>]·1/2(C<sub>5</sub>H<sub>12</sub>): Ti–O<sub>1</sub> 1.893(3), Ti–O<sub>2</sub> 1.898(3), Ti–O<sub>3</sub> 1.831(3), Ti–O<sub>4</sub> 1.848(3), Ti–N<sub>1</sub> 2.270(3), Ti–N<sub>2</sub> 2.279(3), O<sub>1</sub>–C<sub>1</sub> 1.399(5), C<sub>1</sub>–C<sub>2</sub> 1.507(5), N<sub>1</sub>–C<sub>6</sub> 1.347(5), N<sub>1</sub>–C<sub>2</sub> 1.330(5), N<sub>1</sub>–Ti–N<sub>2</sub> 80.7(2), N<sub>1</sub>–Ti–O<sub>4</sub> 165.3(2), O<sub>3</sub>–Ti–O<sub>4</sub> 101.0(2), Ti–O<sub>3</sub>–C<sub>16</sub> 133.5(2), Ti–O<sub>4</sub>–C<sub>13</sub> 132.5(2). For [Ti(13)<sub>2</sub>(OnBu)<sub>2</sub>]: Ti–O<sub>1</sub> 1.915(2), Ti–O<sub>3</sub> 1.825(2), Ti–N<sub>1</sub> 2.254(2), O<sub>1</sub>–C<sub>1</sub> 1.392(4), C<sub>1</sub>–C<sub>2</sub> 1.507(4), N<sub>1</sub>–C<sub>2</sub> 1.337(4), N<sub>1</sub>–C<sub>6</sub> 1.351(4), N<sub>1</sub>–Ti–N<sub>1</sub>′ 82.9(2), N<sub>1</sub>–Ti–O<sub>3</sub> 167.5(2), O<sub>3</sub>–Ti–O<sub>3</sub>′ 99.9(2), Ti–O<sub>3</sub>–C<sub>7</sub> 138.3(2).

When considering 2 alkoxy-substituted pyridine groups as chelates, i.e. 2 nitrogen and 2 oxygen donor atoms, only 33 hits remained. Finally, when only the complexes containing in addition two alkoxido ligands were retained, we found 15 hits for methyloxido groups, 11 hits for ethyloxido groups and only 2 hits for isopropoxido groups,<sup>[17]</sup> including [Ti(13)<sub>2</sub>(OiPr)<sub>2</sub>] which has been previously crystallized in a different space group.<sup>[14,15]</sup> In most of these complexes, the chelating ligands are orthogonal to each other, as observed in this study (Figure 4). The distances and angles around the Ti<sup>IV</sup> center are similar in all these complexes with the following average values: Ti–O-(chelate) 1.93(2) Å, Ti–O(alkoxido) 1.82(2) Å, Ti–N 2.26(2) Å and a N–Ti–N angle of 82(2)°.



**Figure 4.** Typical structural arrangement in *cis*-alkoxy-substituted pyridine Ti<sup>IV</sup> complexes with the N,O chelating ligands orthogonal to each other.

### 2.3. Primary Screening for the Dimerization of Ethylene to 1-Butene

Based on literature data,<sup>[4,7,8]</sup> a standard procedure using 3 equiv. AlEt<sub>3</sub> as co-catalyst was applied to facilitate comparisons between the catalytic properties of the various complexes. The tests were run under 20 bar ethylene at 60 °C, using 6 parallelized 35 mL reactors equipped with ethylene consumption monitoring and mechanical stirring (see ESI, Figure S31). Control experiments were carried out with [Ti(OiPr)<sub>4</sub>] as catalyst to check that all 6 reactors led to the same ethylene uptake (± 0.5 g after 25 min). The reported activities are expressed in grams of ethylene consumed per gram of titanium per hour, based on the ethylene uptake after 25 min. Pressure, temperature and ethylene uptake were monitored (see ESI, Figure S32). The selectivity was determined by gas chromatography. Obviously, these screening experiments having been carried out on a small scale and only very little polymer was formed. A relative, rather than an absolute quantification is still possible that can be used to establish trends in terms of polymer formation.

Following this procedure, all the complexes were found to selectively catalyze the dimerization of ethylene in 1-butene (C<sub>4</sub> > 90% with 99% of 1-C<sub>4</sub>). The results are summarized in Table 1 (the percentage of  $\alpha$ -olefins is given in parentheses) and a graphical view of the screening results is presented in Figure 5.

#### 2.3.1. Influence of the Functional Group

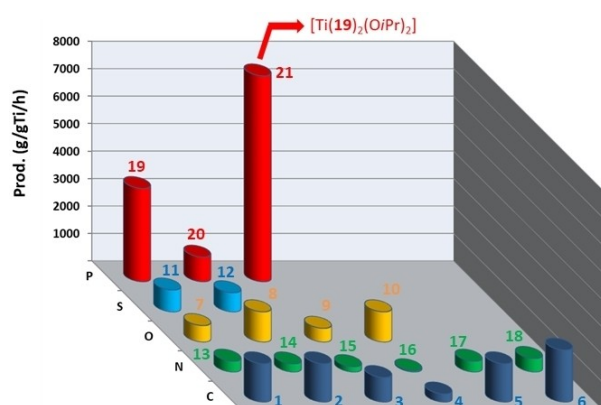
Incorporation of a functional group Z in the alkoxido ligands tends to decrease the catalytic activity compared to [Ti(OiPr)<sub>4</sub>] (entry 1), except in the case of a phosphine function. The activity with ligand **19** (entry 21) was 5 times higher than that of [Ti(OiPr)<sub>4</sub>]. More surprisingly, this increase in activity was accompanied with a quasi-suppression of polymer formation. The soft character of the phosphorous atom cannot be the only parameter responsible for these results since soft sulfur ligands were present in **9** and **10** (entries 11 and 12) which led to low activity and produced larger amount of polymer (> 1%).

The use of ligand **4** (entry 6), which has a diphenyl moiety at a terminal position but no phosphorus atom as in **17**, led to

**Table 1.** Results of the First Screening.<sup>[a]</sup>

Entry	Complex	Activity (g g <sub>Ti</sub> <sup>-1</sup> h <sup>-1</sup> ) <sup>[b]</sup>	Products weight distribution [%]		≥ C <sub>8</sub>	PE <sup>[e]</sup>
			C <sub>4</sub> = (α) <sup>[c]</sup>	C <sub>6</sub> = (α) <sup>[d]</sup>		
1	[Ti(OiPr) <sub>4</sub> ]	1400	93 (99)	6 (9)	< 1	< 1
2	[Ti(OiPr) <sub>4</sub> ] <sup>[f]</sup>	1400	86 (99 <sup>+</sup> )	12 (9)	1	1
3	[Ti(1) <sub>2</sub> (OiPr) <sub>2</sub> ]	900	91 (99)	7 (6)	< 1	1
4	[Ti(2) <sub>2</sub> (OiPr) <sub>2</sub> ]	300	93 (99)	2 (16)	≤ 1	4
5	[Ti(3) <sub>2</sub> (OiPr) <sub>2</sub> ]	1400	94 (99 <sup>+</sup> )	5 (8)	< 1	< 1
6	[Ti(4) <sub>2</sub> (OiPr) <sub>2</sub> ]	1900	92 (99)	7 (6)	–	< 1
7	[Ti(5) <sub>2</sub> (OiPr) <sub>2</sub> ]	600	73 (99 <sup>+</sup> )	25 (4)	1	1
8	[Ti(6) <sub>2</sub> (OiPr) <sub>2</sub> ]	1100	92 (99 <sup>+</sup> )	6 (9)	≤ 1	1
9	[Ti(7) <sub>2</sub> (OiPr) <sub>2</sub> ]	500	95 (99 <sup>+</sup> )	2 (15)	–	2
10	[Ti(8) <sub>2</sub> (OiPr) <sub>2</sub> ]	1100	94.5 (99 <sup>+</sup> )	4 (9)	≤ 1	1
11	[Ti(9) <sub>2</sub> (OiPr) <sub>2</sub> ]	800	95 (99 <sup>+</sup> )	4 (11)	≤ 1	1
12	[Ti(10) <sub>2</sub> (OiPr) <sub>2</sub> ]	700	95 (99 <sup>+</sup> )	3 (12)	≤ 1	1
13	[Ti(11) <sub>2</sub> (OiPr) <sub>2</sub> ]	400	94 (99 <sup>+</sup> )	2 (17)	≤ 1	3
14	[Ti(12) <sub>2</sub> (OiPr) <sub>2</sub> ]	300	98 (99 <sup>+</sup> )	2 (–)	≤ 1	≤ 1
15	[Ti(13) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	200	96 (93)	3 (15)	1	–
16	[Ti(14) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	50	–	–	–	–
17	[Ti(15) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	400	96 (98)	2 (20)	≤ 1	2
18	[Ti(16) <sub>2</sub> (OiPr) <sub>2</sub> ]	500	96 (99 <sup>+</sup> )	3 (13)	≤ 1	1
19	[Ti(17) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[g]</sup>	3400	95 (99 <sup>+</sup> )	4 (12)	< 1	–
20	[Ti(18) <sub>2</sub> (OiPr) <sub>2</sub> ]	900	95 (99)	4 (12)	≤ 1	1
21	[Ti(19) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[g]</sup>	7500	94 (99 <sup>+</sup> )	5 (10)	< 1	≤ 1

[a] Ti precursor (0.15 mmol), AlEt<sub>3</sub> (0.45 mmol), cyclohexane (6 mL), P<sub>C<sub>2</sub>H<sub>4</sub></sub> = 20 bar, T = 60 °C, stirring rate: 1500 rpm, reaction time: 25 min, [b] Expressed in grams of ethylene transformed per gram of Ti per hour (by extrapolating the value at 25 min), [c] 1-Butene vs. total butenes formed, [d] 1-Hexene vs. total hexenes formed, [e] Determined from the solid isolated (insoluble in cyclohexane), [f] Chlorobenzene (6 mL) instead of cyclohexane, [g] Ti precursor (0.075 mmol).

**Figure 5.** Results of the primary screening (labelling refers to entries in Table 1)

an uncontrolled catalytic test with irregular ethylene consumption. In that case, no apparent decrease in polymer formation was observed compared to [Ti(OiPr)<sub>4</sub>]. In contrast, complex [Ti(17)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 19) displayed a higher activity with undetectable polymer formation. These data establish the importance of the phosphorous donor in the ligand, which results in a better control of the reaction and reduces polymer formation. When the functional group associated with the alkoxido ligand contains a nitrogen or oxygen donor, a lower catalytic activity was observed, possibly because of a too strong interaction of these donors with the titanium center. These data suggest that weaker interactions between the functional group Z and titanium, allowing ligand hemilability, might be beneficial for catalysis.<sup>[18]</sup>

### 2.3.2. Influence of the Steric Hindrance

An increase of the steric bulk in α position to the oxygen atom of the functionalized alkoxido ligands dramatically decreased the catalytic activity, as shown with [Ti(2)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 4) and [Ti(18)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 20).

### 2.3.3. Influence of the Spacer Length

An increase in the length of the spacer between the oxygen atom and the heteroatom of the functional group had a beneficial effect on the activity, as shown with the aromatic group of [Ti(3)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 5) vs [Ti(1)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 3) or with the phosphorous group of [Ti(19)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 21) vs [Ti(17)<sub>2</sub>(OiPr)<sub>2</sub>] (entry 19).

### 2.3.4. Influence of the Intramolecular Donor Z and of External Additives

This primary screening revealed that precatalyst [Ti(19)<sub>2</sub>(OiPr)<sub>2</sub>] represents a “hit”. It also showed that a phosphorus-functionalized alkoxido ligand, a longer spacer, and a CH<sub>2</sub> group in α position to the oxygen are beneficial for the selective oligomerization of ethylene. For comparison, external additives were tested with [Ti(OiPr)<sub>4</sub>] to examine the possible influence of intramolecular factors such as ligand chelation (Table 2). All additives led to a strong decrease in activity, except PPh<sub>3</sub> and aromatics. However, this was accompanied by an increase in



**Table 2.** Influence of external additives on catalytic performances. <sup>[a]</sup>

Ti complex	Additive	Activity (g g <sub>Ti</sub> <sup>-1</sup> h <sup>-1</sup> ) <sup>[b]</sup>	Products weight distribution [%]		≥ C <sub>8</sub>	PE <sup>[e]</sup>
			C <sub>4</sub> = (α) <sup>[c]</sup>	C <sub>6</sub> = (α) <sup>[d]</sup>		
[Ti(OiPr) <sub>4</sub> ]	–	1400	93 (99)	6 (9)	< 1	< 1
	Toluene	1100	90 (99+)	9 (9)	≤ 1	1
	Mesitylene	1200	98 (99+)	1 (–)	≤ 1	1
	C <sub>6</sub> Me <sub>6</sub>	1300	90 (99+)	9 (9)	≤ 1	1
	THF	400	97 (99+)	3 (15)	–	–
	MeOBu	600	95 (99)	4 (13)	< 1	≤ 1
	Pyridine	100	99 (99+)	1 (–)	–	–
	PMePh <sub>2</sub>	400	94 (99)	5 (15)	< 1	< 1
	PPh <sub>3</sub>	1000	95 (99)	3 (13)	< 1	< 1
[Ti(4) <sub>2</sub> (OiPr) <sub>2</sub> ]	–	1900	92 (99)	7 (6)	–	< 1
	PPh <sub>3</sub>	2800	94 (99)	6 (10)	≤ 1	≤ 1
[Ti(17) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	–	3400	95 (99+)	4 (12)	< 1	–

[a] Ti precursor (0.15 mmol), additives (0.30 mmol), AlEt<sub>3</sub> (0.45 mmol), cyclohexane (6 mL), P<sub>C<sub>2</sub>H<sub>4</sub></sub> = 20 bar, T = 60 °C, stirring rate: 1500 rpm, reaction time: 25 min. [b] Expressed in grams of ethylene transformed per gram of Ti per hour (by extrapolating the value at 25 min). [c] 1-Butene vs. total butenes formed. [d] 1-Hexene vs. total hexenes formed. [e] Determined from the solid isolated at the end of the reaction (insoluble in cyclohexane). [f] Ti precursor (0.075 mmol).

selectivity toward 1-butene. PPh<sub>3</sub> was the only additive that led to increased selectivity with only a slight decrease in activity.

It is noteworthy that none of the additives tested with [Ti(OiPr)<sub>4</sub>] led to an activity and selectivity comparable to those of [Ti(19)<sub>2</sub>(OiPr)<sub>2</sub>], which is clearly consistent with the beneficial effects of an internal functionalization of the alkoxido ligands. Even the addition of 2 equiv. of PPh<sub>3</sub> to [Ti(4)<sub>2</sub>(OiPr)<sub>2</sub>] did not allow to reach the activity of [Ti(17)<sub>2</sub>(OiPr)<sub>2</sub>], which is again consistent with the beneficial involvement of intramolecular effects. By decreasing the catalytic activity of the system, the addition of PPh<sub>3</sub> reduces the exothermicity of the reaction which probably explains the reduction of polymer formation.

## 2.4. Focused Alkoxido-Phosphorus Ligands Library and Secondary Screening

### 2.4.1. Synthesis of the Titanium Complexes

The objective of this secondary screening was to explore an area of the experimental space close to the hit [Ti(19)<sub>2</sub>(OiPr)<sub>2</sub>]. Ligands of greater structural diversity were then synthesized (Figure 6). Following the protocol described in [Eq. (1)], we prepared the precursor 20·H, with 4 methylene units forming a linear spacer between the hydroxy and the diphenylphosphino groups. We also introduced a cyclic spacer with the proligands 21·H<sup>[19]</sup> and 22·H.<sup>[20]</sup> Further modifications of the phosphorus stereoelectronic properties were brought about with proligand 23·H.<sup>[11,12]</sup> In that case, replacing a phenyl with a methyl substituent on the phosphorus led to a shift of the <sup>31</sup>P NMR resonance from –16.3 to –35.4 ppm, consistent with the increased basicity of the phosphorus donor. Unfortunately, attempts to synthesize dialkylphosphinoalcohols in order to extend the electronic diversity of this library were unsuccessful. We finally introduced the new ligand precursors 24·H and 25·H, the oxide and sulfide derivatives of 19·H, respectively.

Access to the new titanium complexes based on the focused ligand precursors library was achieved according to the

general synthetic procedure of [Eq. (1)]. However, when both the functional alcohol and the complexes were insoluble in cyclohexane, the reaction did not proceed, and cyclohexane was replaced by dichloromethane. Di-substitution affording [Ti(OR)<sub>2</sub>(OiPr)<sub>2</sub>] occurred in all cases. Most complexes displayed rather broad <sup>1</sup>H NMR signals (Figures S2–S30 in ESI), suggesting that polynuclear structures with bridging alkoxido (functionalized or not) ligands may be present in solution. Consistently, the <sup>31</sup>P NMR spectra of complexes containing ligands 21, 22 and 24 displayed weaker additional resonances or a multiplet (see e.g. Figure S26 in ESI), possibly indicating an interaction with titanium and/or the occurrence of an equilibrium between mononuclear and dinuclear structures. For the complex obtained from 21·H, the complex <sup>31</sup>P NMR signals may be due to the presence of stereoisomers. A <sup>31</sup>P chemical shift for a titanium complex close to that of the alcohol precursor is consistent with no or weak interaction between the phosphorus and the titanium center.

### 2.4.2. Catalytic Evaluation

The general ethylene dimerization test described for the primary screening was applied to this new library of complexes, using cyclohexane as solvent and 3 equiv. of AlEt<sub>3</sub> as co-catalyst (Table 3). For complexes that were poorly soluble or insoluble in cyclohexane, catalytic testing was performed in chlorobenzene. We assumed little to no impact of this solvent on the catalytic productivity of [Ti(OR)<sub>2</sub>(OiPr)<sub>2</sub>], as justified by the example of [Ti(OiPr)<sub>4</sub>] (Table 3, entries 1 and 2). Slight changes in products distribution may be caused by the nature of the solvent and associated differences of ethylene solubility, resulting in variations of ethylene conversion.

All catalytically active complexes dimerized ethylene in 1-butene. The lengthening of the linker from a propyl (19) to a butyl chain (20) led a more active complex with similar selectivity (Table 3, entries 5 and 6). The activity of [Ti(20)<sub>2</sub>(OiPr)<sub>2</sub>] was found to be 8 times higher than that of

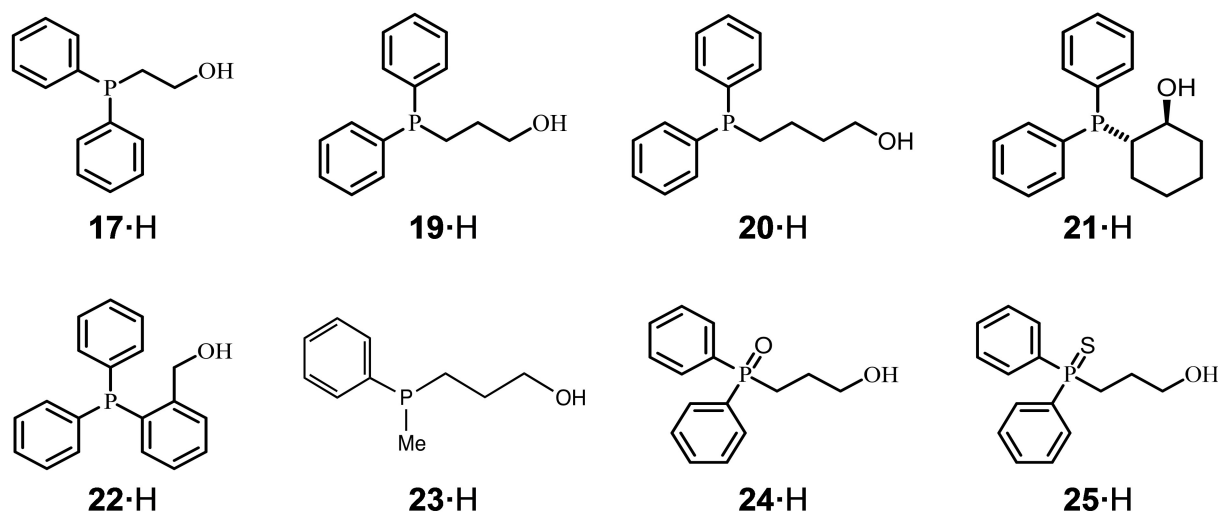
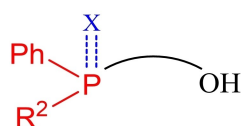


Figure 6. Focused ligand precursors library.  $R^2 = \text{Ph}$  or  $\text{Me}$ ;  $X = \text{O}$  or  $\text{S}$ .

Table 3. Results of the secondary screening.<sup>[a]</sup>

Entry	Complex	Activity [g g <sub>Ti</sub> <sup>-1</sup> h <sup>-1</sup> ] <sup>[b]</sup>	Products weight distribution [%]			
			C <sub>4</sub> <sup>=</sup> (α) <sup>[c]</sup>	C <sub>6</sub> <sup>=</sup> (α) <sup>[d]</sup>	≥ C <sub>8</sub>	PE <sup>[e]</sup>
1	[Ti(OiPr) <sub>4</sub> ]	1400	93 (99)	6 (9)	< 1	< 1
2	[Ti(OiPr) <sub>4</sub> ] <sup>[f]</sup>	1400	86 (99 <sup>+</sup> )	12 (9)	1	1
4	[Ti(17) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[g]</sup>	3400	95 (99 <sup>+</sup> )	4 (12)	< 1	–
5	[Ti(19) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[g]</sup>	7500	94 (99 <sup>+</sup> )	5 (10)	< 1	≪ 1
6	[Ti(20) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[g]</sup>	11600 <sup>[h]</sup>	92 (99 <sup>+</sup> )	7 (8)	< 1	≪ 1
7	[Ti(21) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	800	95 (99)	2 (15)	< 1	1
8	[Ti(22) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	300	88 (98)	6 (14)	1	5
9	[Ti(23) <sub>2</sub> (OiPr) <sub>2</sub> ]	2400	96 (99 <sup>+</sup> )	3 (18)	< 1	–
10	[Ti(24) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	100	99 <sup>+</sup>	–	–	–
11	[Ti(25) <sub>2</sub> (OiPr) <sub>2</sub> ] <sup>[f]</sup>	0	–	–	–	–

[a] Ti precursor (0.15 mmol), AlEt<sub>3</sub> (0.45 mmol), cyclohexane (6 mL), P<sub>C<sub>2</sub>H<sub>4</sub></sub> = 20 bar, T = 60 °C, stirring rate: 1500 rpm, reaction time: 25 min. [b] Expressed in grams of ethylene transformed per gram of Ti per hour (by extrapolating the value at 25 min). [c] 1-Butene vs. total butenes formed. [d] 1-Hexene vs. total hexenes formed. [e] Determined from the solid isolated (insoluble in cyclohexane). [f] chlorobenzene (6 mL) instead of cyclohexane. [g] Ti precursor (0.075 mmol). [h] Maximum ethylene consumption reached after 15 min.

[Ti(OiPr)<sub>4</sub>]. When a diphenylphosphino group (17) was replaced with methylphenylphosphino group (23), the activity decreased, highlighting again the importance of the -PPh<sub>2</sub> groups on the activity (Table 3, entries 4 and 9). When the P<sup>III</sup> donor of the Z function was replaced with a P<sup>V</sup> atom, as in the oxide (24) or sulfide (25) derivatives, the beneficial “phosphorus effect” on activity and selectivity was suppressed, leading to inactive catalysts. Ligands 21 and 22 with cyclic linkers (aromatic or not) also led to less active catalysts. Thus, a flexible linker between the oxygen and the phosphorus donors appears highly beneficial for catalysis.

## 2.5. Final Optimization of the Catalyst Formulation

### 2.5.1. Influence of the Alkoxido Co-ligands

In all the complexes of type [Ti(OR)<sub>2</sub>(OiPr)<sub>2</sub>] discussed so far, only isopropoxido co-ligands were used in combination with functionalized alkoxido ligands. A comparison of the productivities of [Ti(OnBu)<sub>4</sub>] and [Ti(OiPr)<sub>4</sub>] indicates that linear alkoxy co-ligands lead to better conversion than branched ones.<sup>[4]</sup> This observation is consistent with the results of our primary screening demonstrating the negative impact of steric hindrance at the α-position to the O<sub>Ti</sub> on productivity.



Thus, a new set of complexes was synthesized starting from  $[\text{Ti}(\text{OnBu})_4]$  and containing the linear diphenylphosphino-alkoxido ligands **17**, **19** and **20**, identified as the best ligands up to now. The respective complexes  $[\text{Ti}(\text{17})_2(\text{OnBu})_2]$ ,  $[\text{Ti}(\text{19})_2(\text{OnBu})_2]$  and  $[\text{Ti}(\text{20})_2(\text{OnBu})_2]$  were obtained in quantitative yields from the corresponding alcohols according to [Eq. (1)]. These complexes revealed even broader  $^1\text{H}$  NMR signals compared to the other complexes synthesized. This may indicate that polynuclear structures with bridging alkoxido ligands are present in solution. Increasing the temperature appears to break these bridges, as shown by a sharpening of the  $^1\text{H}$  NMR signals of  $[\text{Ti}(\text{19})_2(\text{OnBu})_2]$  at  $60^\circ\text{C}$  in toluene- $d_8$  (Figure S23 in ESI), where the broad signal at 4.3 ppm is split in two different signals. A COSY(H,H) experiment allowed to assign each resonance to either the  $\text{CH}_2$  of the butoxido ligand or the  $\text{CH}_2$  of the phosphorus functionalized ligand. The  $^{31}\text{P}$  spectrum contained a single peak at  $-16.0$  ppm (vs  $-16.1$  ppm for **19**·H), which is consistent with a dangling phosphorus atom.

The complexes of general formula  $[\text{Ti}(\text{OR})_2(\text{OnBu})_2]$  were evaluated for ethylene dimerization and compared to the corresponding precatalysts  $[\text{Ti}(\text{OR})_2(\text{OiPr})_2]$  (Table 4). A contrasting effect of the co-ligand linearity was observed. We firstly noticed an important increase in activity when  $[\text{Ti}(\text{17})_2(\text{OnBu})_2]$  and  $[\text{Ti}(\text{19})_2(\text{OnBu})_2]$  were compared to  $[\text{Ti}(\text{17})_2(\text{OiPr})_2]$  and

$[\text{Ti}(\text{19})_2(\text{OiPr})_2]$ , respectively (entries 1 to 4). A slight decrease of the productivity was however observed for  $[\text{Ti}(\text{20})_2(\text{OnBu})_2]$  when compared to  $[\text{Ti}(\text{20})_2(\text{OiPr})_2]$  (entries 5 and 6). Finally, the use of 2 equiv.  $\text{PPh}_3$  as additive with  $[\text{Ti}(\text{OnBu})_4]$  led to lower performances than  $[\text{Ti}(\text{20})_2(\text{OnBu})_2]$ , providing further evidence for the beneficial effect of an internal functionalization of the alkoxido ligand. Complex  $[\text{Ti}(\text{19})_2(\text{OnBu})_2]$  proved to be the best catalyst tested and thus was qualified as “lead” of this secondary screening.

## 2.5.2. Influence of the Co-catalyst

At this stage, we wanted to check whether  $\text{AlEt}_3$  was the best co-catalyst.<sup>[5,9]</sup> Thus, a screening of various co-catalysts ( $\text{AlMe}_3$ ,  $\text{AlEt}_2\text{Cl}$ ,  $\text{AlEtCl}_2$ ,  $\text{Al}_2\text{Et}_3\text{Cl}_3$  and MAO) was performed with complex  $[\text{Ti}(\text{19})_2(\text{OnBu})_2]$ , the “lead” pre-catalyst of the secondary screening, in order to determine the best conditions for high activity, good selectivity for 1-butene without polymer formation (Table 5).

All the chlorinated activators ( $\text{Al/Ti}=3$ , 20 or 40) only gave polymers, like MAO ( $\text{Al/Ti}=900$ ), whatever the  $\text{Al/Ti}$  ratio employed.  $\text{AlMe}_3$  led to higher selectivity but lower activity.

**Table 4.** Oligomerization of ethylene using  $[\text{Ti}(\text{OR})_2(\text{OnBu})_2]$  and  $[\text{Ti}(\text{OR})_2(\text{OiPr})_2]$  as precatalysts.<sup>[a]</sup>

Entry	Complex	Activity [ $\text{g g}_{\text{Ti}}^{-1} \text{h}^{-1}$ ] <sup>[b]</sup>	Products weight distribution [%] $C_4 = (\alpha)^{[c]}$	$C_6 = (\alpha)^{[d]}$	$\geq C_8$	PE <sup>[e]</sup>
1	$[\text{Ti}(\text{17})_2(\text{OiPr})_2]^{[f]}$	3400	95 (99+)	4 (12)	< 1	–
2	$[\text{Ti}(\text{17})_2(\text{OnBu})_2]^{[f]}$	5500	94 (99)	5 (11)	< 1	$\leq 1$
3	$[\text{Ti}(\text{19})_2(\text{OiPr})_2]^{[f]}$	7500	94 (99+)	5 (10)	< 1	$\leq 1$
4	$[\text{Ti}(\text{19})_2(\text{OnBu})_2]^{[f]}$	13000 <sup>[g]</sup>	93 (99+)	6 (10)	< 1	$\leq 1$
5	$[\text{Ti}(\text{20})_2(\text{OiPr})_2]^{[f]}$	11600 <sup>[g]</sup>	92 (99+)	7 (8)	< 1	$\leq 1$
6	$[\text{Ti}(\text{20})_2(\text{OnBu})_2]^{[f]}$	9500	92 (99+)	7 (8)	< 1	$\leq 1$
7	$[\text{Ti}(\text{OnBu})_4] / 2 \text{ PPh}_3$	3800	94 (99)	6 (5)	–	$\leq 1$

[a] Ti precursor (0.15 mmol),  $\text{AlEt}_3$  (0.45 mmol), cyclohexane (6 mL),  $P_{\text{C}_2\text{H}_4}=20$  bar,  $T=60^\circ\text{C}$ , stirring rate: 1500 rpm, reaction time: 25 min. [b] Expressed in grams of ethylene transformed per gram of Ti per hour (by extrapolating the value at 25 min). [c] 1-Butene vs. total butenes formed. [d] 1-Hexene vs. total hexenes formed. [e] Determined from the solid isolated (insoluble in cyclohexane). [f] Ti precursor (0.075 mmol). [g] Maximum ethylene consumption reached after 15 min.

**Table 5.** Co-catalyst screening using  $[\text{Ti}(\text{19})_2(\text{OnBu})_2]$ .<sup>[a]</sup>

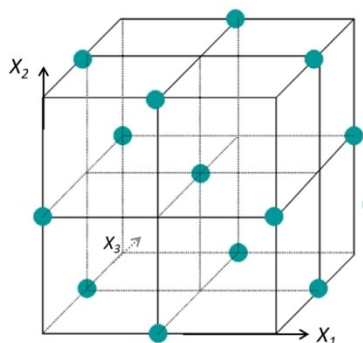
Co-catalyst	Al/Ti ratio	Activity [ $\text{g g}_{\text{Ti}}^{-1} \text{h}^{-1}$ ] <sup>[b]</sup>	Products weight distribution [%] $C_4 = (\alpha)^{[c]}$	$C_6 = (\alpha)^{[d]}$	$\geq C_8$	PE <sup>[e]</sup>
$\text{AlEt}_3$	3 <sup>[f]</sup>	13000 <sup>[g]</sup>	93 (99+)	6 (10)	< 1	$\leq 1$
$\text{AlMe}_3$	3 <sup>[h]</sup>	8600	97 (99+)	3 (7)	$\leq 1$	$\leq 1$
$\text{AlEt}_2\text{Cl}$	3	< 100	–	–	–	–
	20	600	< 1	< 1	< 1	99
$\text{Al}_2\text{Et}_3\text{Cl}_3$	3 <sup>[h]</sup>	< 100	–	–	–	–
	20	600	< 1	< 1	< 1	99
	40	1000	< 1	< 1	< 1	99
$\text{AlEtCl}_2$	3 <sup>[h]</sup>	< 100	–	–	–	–
	20	900	< 1	< 1	< 1	99
	40	1200	< 1	< 1	< 1	99
MAO <sup>[i]</sup>	3	< 100	–	–	–	–
	900	2500	< 1	< 1	< 1	99

[a] Ti precursor (0.05 mmol), cyclohexane (6 mL),  $P_{\text{C}_2\text{H}_4}=20$  bar,  $T=60^\circ\text{C}$ , stirring rate: 1500 rpm, reaction time: 25 min. [b] Expressed in grams of ethylene transformed per gram of Ti per hour (by extrapolating the value at 25 min). [c] 1-Butene vs. total butenes formed. [d] 1-Hexene vs. total hexenes formed. [e] Determined from the solid isolated (insoluble in cyclohexane). [f] Ti precursor (0.075 mmol). [g] Maximum ethylene consumption reached after 15 min. [h] Ti precursor (0.04 mmol). [i] Ti precursor (0.01 mmol).

AlEt<sub>3</sub> was then selected for the screening of the experimental parameters (see below).

## 2.6. Optimization of the Operating Conditions by Design of Experiments (DoE)

When a large number of parameters controlling a catalytic reaction need to be evaluated and optimized, a Design of Experiment (DoE) approach is a highly valuable strategy to find cause-and-effect relationships and identify the optimum catalytic conditions.<sup>[21]</sup> By maximizing the amount of information while minimizing the number of experiments to be performed, this approach is far more efficient than traditional methods involving consecutive optimization of numerous reaction parameters. The DoE methodology relies on a mathematical model (here a second-degree polynomial model), with a predicting variance as small as possible, that connects a response  $Y_i$  (or output variable) with  $J$  factors  $X_j$  (or input variables), etc, starting from a small number of experiments.



**Figure 7.** Representation of Box-Behnken matrix for the 3 parameters studied ( $X_1$ – $X_3$ )

This model is valid within the domain D of feasible experiments. Since their number is generally very high, it is important to properly select them in order to limit costs and time of execution.<sup>[22]</sup> In this work, we decided to use standard designs for response surfaces analysis, more precisely the Box-Behnken matrix. The critical parameters and their variations considered here are the pressure ( $10 \text{ bar} < X_1 < 30 \text{ bar}$ ), the temperature ( $40 < X_2 < 80^\circ\text{C}$ ) and the AlEt<sub>3</sub>/Ti ratio ( $2 < X_3 < 6$ ). An experimental space with selected points (or experiments to be done) can be built based on the Box-Behnken matrix (Figure 7).

With a Box-Behnken design, 13 experiments were necessary to identify the polynomial model. The experiment in the center of the matrix was reproduced 3 times for statistics on the DoE. Finally, 3 catalytic tests were added for model evaluation. The results of the DoE are reported in Table 6.

Only small variations of C<sub>4</sub>, C<sub>6</sub> and C<sub>8</sub> selectivities were observed. An increased reaction temperature was found to result in a higher activity but also in polymer formation (entries 11 and 12 for example). Catalyst deactivation was faster at higher temperature. Polymer formation is also favored by increasing the Al/Ti ratio (e.g. entries 5 and 7). As expected, an increased ethylene pressure resulted in an improved activity with, however, no apparent change in selectivity (e.g. entries 1 and 2). Due to the lack of variations in selectivity, only productivities were taken into account for polynomial modeling and surface response analysis. Mathematical details are presented in the ESI (Figure S33). A plot of the predicted vs experimental productivities demonstrates the good quality of the model (Figure 8). Dotted lines represent the parallels of the model passing through the minimum and maximum values of activity at the center revealing that all the blue points are in between. Even if the model was not able to predict really well the activity of the entries 16–18 (in pink), it localized them in the right area.

**Table 6.** Results of the box-Behnken design of experiments and screening with [Ti(19)<sub>2</sub>(OnBu)<sub>2</sub>].<sup>[a]</sup>

Entry	P (bar)	T (°C)	Al/Ti	Activity [g g <sub>Ti</sub> <sup>-1</sup> h <sup>-1</sup> ] <sup>[b]</sup>	Sel. C <sub>4</sub> [%wt]	Sel. C <sub>6</sub> [%wt]	Sel. C <sub>8</sub> [%wt]	%PE <sup>[c]</sup>
1 (model)	10	40	4	5200	93	7	<1	0.0
2 (model)	30	40	4	10000	96	4	<1	0.0
3 (model)	10	80	4	7500	82	17	2	0.0
4 (model)	30	80	4	12200 <sup>[d]</sup>	94	6	<1	0.1
5 (model)	10	60	2	2100	93	7	<1	0.0
6 (model)	30	60	2	4200	96	4	<1	0.0
7 (model)	10	60	6	6600	91	8	<1	0.7
8 (model)	30	60	6	14300 <sup>[d]</sup>	95	3	<1	1.5
9 (model)	20	40	2	3200	97	3	<1	0.0
10 (model)	20	80	2	1300	95	5	<1	0.0
11 (model)	20	40	6	8100	93	6	<1	0.6
12 (model)	20	80	6	4600	92	3	<1	4.6
13 (center)	20	60	4	10300	90	9	<1	0.2
14 (center)	20	60	4	11800	89	10	<1	0.1
15 (center)	20	60	4	11200	93	7	<1	0.1
16 (test)	15	70	3	7400	93	7	<1	0.0
17 (test)	25	50	5	14700 <sup>[d]</sup>	94	5	<1	0.3
18 (test)	25	70	3	10500 <sup>[d]</sup>	96	4	<1	0.0

[a] Ti precursor (0.075 mmol), cyclohexane (6 mL), stirring rate: 1500 rpm, reaction time: 15 min. [b] Expressed in grams of ethylene transformed per gram of Ti per hour (by extrapolating the value at 25 min). [c] Determined from the solid isolated (insoluble in cyclohexane). [d] Ti precursor (0.04 mmol).

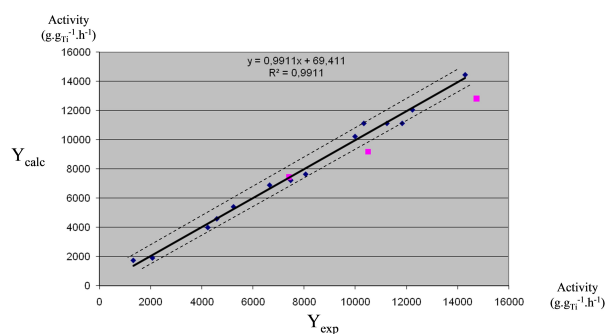


Figure 8. Modelled vs experimental productivity.

### 3. Conclusion

In the search for homogeneous catalysts allowing the selective and efficient dimerization of ethylene to 1-butene, a library of titanium complexes of the type  $[\text{Ti}(\text{OR})_2(\text{O}i\text{Pr})_2]$  and  $[\text{Ti}(\text{OR})_2(\text{O}n\text{Bu})_2]$  (not all combinations), where OR represents a functionalized alkoxido ligand, was synthesized and characterized. These alkoxido ligands contain a functional end-group Z and were introduced in the titanium coordination sphere by selective reaction of the corresponding aromatic-, oxygen-, nitrogen-, sulfur- and phosphorus-functionalized alcohols with  $[\text{Ti}(\text{O}i\text{Pr})_4]$ . Considering the number of variables to be optimized, such as the nature of the functionality Z carried by the alkoxido ligands –OR, the length of the spacer between Z and the alkoxido oxygen atom, the steric hindrance around this oxygen atom, the role of the co-ligands (*OiPr* or *OnBu*), the nature and ratio of the co-catalyst, the reactions conditions, we performed a three-steps investigations involving High Throughput Screening (HTS) and Design of Experiment (DoE) approaches. A primary screening of the catalyst performances in oligomerization of ethylene using 3 equiv. of  $\text{AlEt}_3$ , at 20 bar and 60 °C, showed that all complexes selectively dimerized ethylene to 1-butene. The best activities were obtained with a phosphorus-functionalized alkoxido ligand with a linear and long enough spacer to allow direct interaction between Z and the titanium center. A secondary screening was then performed on a library focused on this “hit” and revealed that a diphenylphosphino-functionalized alkoxido ligand with a 3 carbon atoms spacer gave the best results when associated with *n*-butoxido co-ligands on titanium. Operating conditions to be used for this “lead” catalyst were optimized through a Box-Behnken design of experiments. A good model for the activity was found and helped to identify the best catalytic conditions. Sequential optimization led to identify  $[\text{Ti}(\mathbf{19})_2(\text{O}n\text{Bu})_2]$  as the best precatalyst, selectively dimerizing ethylene in 1-butene ( $C_4(\alpha) = 93\%$  ( $99^+\%$ )) at 30 bar  $C_2H_4$  and 55 °C with  $\text{AlEt}_3$  as co-catalyst and leading to very high activity for a homogeneous titanium catalyst ( $13000 \text{ g}_{\text{Ti}}^{-1} \text{ h}^{-1}$ ). We believe that this study has not only allowed to identify an excellent catalyst for the reaction investigated but also shown the usefulness of combining High Throughput Screening (HTS) and Design of Experiment (DoE) approaches.

## Experimental Section

### General

All experiments were performed under an argon atmosphere using standard Schlenk techniques. All stirring rods were in glass. Anhydrous THF,  $\text{Et}_2\text{O}$ , pentane, dichloromethane and toluene were purified by a solvent purification system (SPS-M-Braun) and cyclohexane was distilled over sodium. Their water content was determined by the Karl-Fischer method using a microcoulometer Methrom 756 KF. Anhydrous ethanol, methanol and chloroform were stored over 4 Å molecular sieves. All solvents were purchased from Sigma-Aldrich, Fluka, Acros, Alfa Aesar or Carlo-Erba. All reagents were purchased from Sigma-Aldrich or Strem and used as received unless otherwise specified.  $[\text{Ti}(\text{O}i\text{Pr})_4]$ ,  $[\text{Ti}(\text{O}n\text{Bu})_4]$  and  $\text{PPh}_2\text{Cl}$  were distilled and kept under argon. Deuterated solvents ( $\text{CDCl}_3$ , toluene- $d_8$  and  $\text{CD}_2\text{Cl}_2$ ) were purchased from Sigma-Aldrich or Eurisotop. The solvents were freeze-pumped and stored over 4 Å molecular sieves under argon. All stirrer bars were in glass.

NMR spectra were recorded on a Bruker AC 300 MHz at 293 K unless otherwise stated. All chemical shifts are reported in ppm vs  $\text{SiMe}_4$  and were determined with reference to residual solvent peaks.  $^{31}\text{P}$  NMR chemical shifts are reported in ppm related to a 85%  $\text{H}_3\text{PO}_4$  solution in water. All coupling constants are given in Hertz. The IR spectra were measured on a Perkin-Elmer Spectrum One FT-IR spectrometer equipped with a ZnSe diamond ATR. GC analyses were performed on an Agilent 6850 series II or Varian CP-3800 equipped with autosamplers and fitted with PONA columns. GC-MS analyses were performed on an Agilent 6890 N equipped with an autosampler and fitted with a PONA or HP-5-MS column and an Agilent 5975B inert XL EI/CI MSD mass spectrometer. Elemental analyses were performed by the Service Central d'Analyses of CNRS (Vernaison, France) or by the ICM-Université de Bourgogne (Dijon, France). X-ray diffraction analyses performed in Strasbourg used a Kappa CCD diffractometer with graphite-monochromated  $\text{Mo-K}\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). Data were collected using  $\Psi$  scans, the structures were solved by direct methods using the SHELX97 software,<sup>[23,24]</sup> and the refinement was by full-matrix least squares on  $F^2$ , using the OLEX2 software.<sup>[25]</sup> No absorption correction was used. All non-hydrogen atoms were refined anisotropically, with H atoms introduced as fixed contributors ( $d_{\text{C-H}} = 0.95 \text{ \AA}$ ,  $U_{11} = 0.04$ ) (Table 7). Diffraction data obtained at the Université Claude Bernard-Lyon I were collected on a Nonius Kappa CCD diffractometer using  $\text{Mo-K}\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). Data were collected using  $\Psi$  scans; the structure was solved by direct methods using the SIR97 software and was refined by full-matrix least squares on  $F^2$ . No absorption correction was used (Table 7). High resolution (200 000 FWHM) mass spectra were acquired with a FT-ICR/MS instrument (Thermo Scientific LTQ-FT Ultra).

The compounds 2-diphenylphosphinoethanol ( $\mathbf{17}\cdot\text{H}$ ),<sup>[11]</sup> 1-diphenylphosphino-2-methylpropan-2-ol ( $\mathbf{18}\cdot\text{H}$ ),<sup>[11]</sup> *trans*-2-(diphenylphosphino)cyclohexanol ( $\mathbf{21}\cdot\text{H}$ )<sup>[19]</sup> and 2-(diphenylphosphinophenyl)methanol ( $\mathbf{22}\cdot\text{H}$ )<sup>[20]</sup> were synthesized according to literature procedures. The synthesis and characterization of the ligand precursors and of the metal complexes are detailed in the Supporting Information.

### Catalytic Ethylene Oligomerization

Studies were performed in a 6-parallel semi-batch autoclaves equipment (T239, see ESI Figure S31). The reactors were placed under an inert atmosphere of nitrogen before the cyclohexane, the complex (0.15 mmol, 1.0 equiv.) and  $\text{AlEt}_3$  (0.45 mmol, 3.0 equiv.) were added. The total volume of solutions introduced was 6 mL.

**Table 7.** Crystallographic Data and Structure Refinement Details.

	19·H	[Ti(13) <sub>2</sub> (O <sup>i</sup> Pr) <sub>2</sub> ]·0.5(C <sub>5</sub> H <sub>12</sub> )	[Ti(13) <sub>2</sub> (OnBu) <sub>2</sub> ]
Formula	C <sub>15</sub> H <sub>17</sub> OP	C <sub>18</sub> H <sub>26</sub> N <sub>2</sub> O <sub>4</sub> Ti <sub>1.5</sub> (C <sub>5</sub> H <sub>12</sub> )	C <sub>20</sub> H <sub>30</sub> N <sub>2</sub> O <sub>4</sub> Ti
Crystal System	Monoclinic	Monoclinic	Monoclinic
Space group	<i>P</i> 2 <sub>1</sub> /c	<i>C</i> 2/c	<i>C</i> 2/c
<i>a</i> (Å)	13.020(2)	22.1124(10)	12.4675(7)
<i>b</i> (Å)	5.396(1)	15.5077(10)	11.4163(4)
<i>c</i> (Å)	19.397(3)	16.0784(10)	14.7623(8)
$\alpha$ (°)	90.00	90.00	90.00
$\beta$ (°)	107.40(2)	130.812(3)	95.750(2)
$\gamma$ (°)	90.00	90.00	90.00
Cell volume (Å <sup>3</sup> )	1300.4(4)	4172.9(5)	2090.59
Density	1.248	1.332	1.304
$\mu$ (mm <sup>−1</sup> )	0.192	0.438	0.436
<i>Z</i>	4	8	4
<i>F</i> (000)	520	1787.133	872
<i>T</i> (K)	100	173	173
$\Theta_{\min}$ , $\Theta_{\max}$ (°)	3.75, 29.36	1.79, 27.46	2.48, 27.48
− <i>h</i> / <i>h</i>	−16/17	−21/21	−16/15
− <i>k</i> / <i>k</i>	−5/7	−20/18	−14/12
− <i>l</i> / <i>l</i>	−25/26	−20/15	−19/14
Measd. reflections	8739	10561	6389
Indep. reflections	3146	4132	2384
<i>R</i> <sub>int</sub>	0.039	0.0355	0.0588
<i>R</i> [ <i>F</i> <sup>2</sup> > 2 $\sigma$ ( <i>F</i> <sup>2</sup> )]	0.0573	0.0765	0.0641
<i>wR</i> ( <i>F</i> <sup>2</sup> ) [ <i>F</i> <sup>2</sup> > 2 $\sigma$ ( <i>F</i> <sup>2</sup> )]	0.1149	0.2271	0.1747
<i>R</i> (all data)	0.0736	0.0997	0.0749
<i>wR</i> ( <i>F</i> <sup>2</sup> ) (all data)	0.1410	0.2557	0.1864
GOOF	0.96	1.0565	1.031
$\Delta\rho_{\min}$ , $\Delta\rho_{\max}$ (e Å <sup>−3</sup> )	−0.84, 0.52	−1.41, 2.01	−0.58, 1.10

The ethylene pressure was immediately increased to 20 bar and the temperature to 60 °C. The mechanical stirring was then set to 1500 rpm and the ethylene uptake was measured. Special attention was paid to the uptake at 25 min which was used to calculate the activity. The test was stopped after 1 h or after 10 g of ethylene was consumed, whichever occurred first. The autoclave was then cooled to room temperature and depressurized. The liquid phase was collected (by pipette after the autoclave was opened) and weighed. After quenching with a 10% H<sub>2</sub>SO<sub>4</sub> solution in water (1 mL), the organic layer was analyzed by GC. The polymer formed was dried overnight in air and weighted.

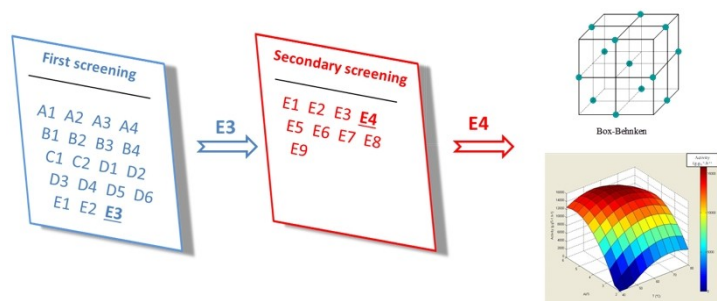
## Acknowledgments

We thank the ANRT (PhD grant CIFRE) and IFP Energies Nouvelles for financial support and Drs. Roberto Pattacini and Lydia BreLOT (Université de Strasbourg) and Erwann Jeanneau (Université Claude Bernard – Lyon 1) for the crystal structure determinations. We also thank S. Harry and D. Proriot for technical support.

**Keywords:** Design of Experiment • Catalytic Ethylene Dimerization • Functional Alkoxides • High Throughput Screening • Ti complexes.

- [1] a) M. Renon-Carrasco, L. Lefort, *Chem. Soc. Rev.*, **2018**, *47*, 5038–5060; b) E. S. Isbrandt, R. J. Sullivan, S. G. Newman, *Angew. Chem. Int. Ed.* **2019**, *58*, 7180–7191; c) K. McCullough, T. Williams, K. Mingle, P. Jamshidi, J. Lauterbach, *Phys. Chem. Chem. Phys.* **2020**, *22*, 11174–11196; d) A. Gordillo, S. Tittlbach, C. Futter, M. L. Lejkowski, E. Prasetyo, L. T. A. Rupflin, T. Emmert, S. A. Schunk, From *Ullmann's Encyclopedia of Industrial Chemistry* **2014**, 7<sup>th</sup> Edition, Edt. B. Elvers.
- [2] a) J. Tian, G. W. Coates, *Angew. Chem. Int. Ed.* **2000**, *39*, 3626–3629; *Angew. Chem.* **2000**, *112*, 3772–3775; b) M. T. Reetz, *Angew. Chem. Int. Ed.* **2002**, *41*, 1335–138; *Angew. Chem.* **2002**, *114*, 1391–1394; c) D. J. Jones, V. C. Gibson, S. M. Green, P. J. Maddox, *Chem. Commun.* **2002**, 1038–1039; d) V. Murphy, X. H. Bei, T. R. Boussie, O. Brummer, G. M. Diamond, C. Goh, K. A. Hall, A. M. Lapointe, M. Leclerc, J. M. Longmire, J. A. W. Shoemaker, H. Turner, W. H. Weinberg, *Chem. Rev.* **2002**, *2*, 278–289; e) V. Murphy, A. F. Volpe, W. H. Weinberg, *Curr. Opin. Chem. Biol.* **2003**, *7*, 427–433; f) T. R. Boussie, G. M. Diamond, C. Goh, K. A. Hall, A. M. LaPointe, M. Leclerc, C. Lund, V. Murphy, J. A. W. Shoemaker, U. Tracht, H. Turner, J. Zhang, T. Uno, R. K. Rosen, J. C. Stevens, *J. Am. Chem. Soc.* **2003**, *125*, 4306–4317; g) N. Adams, H. J. Arts, P. D. Bolton, D. Cowell, S. R. Dubberley, N. Friederichs, C. M. Grant, M. Kranenburg, A. J. Sealey, B. Wang, P. J. Wilson, A. R. Cowley, P. Mountford, M. Schroder, *Chem. Commun.* **2004**, 434–435; h) D. J. Jones, V. C. Gibson, S. M. Green, P. J. Maddox, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **2005**, *127*, 11037–11046; i) D. C. Webster, *Macromol. Chem. Phys.* **2008**, *209*, 237–246; j) M. Delferro, T. J. Marks, *Chem. Rev.* **2011**, *111*, 2450–2485; k) E. Y. X. Chen, T. J. Marks, *Chem. Rev.* **2000**, *100*, 1391–1434; l) C. Ehm, A. Mingione, A. Vittoria, F. Zaccaria, R. Cipullo, V. Busico, *Ind. Eng. Chem. Res.* **2020**, *59*, 13940–13947; m) C. Ehm, A. Vittoria, G. P. Goryunov, V. V. Izmer, D. S. Kononovich, O. V. Samsonov, R. Di Girolamo, P. H. M. Budzelaar, A. Z. Voskoboynikov, V. Busico, D. V. Uborsky, R. Cipullo, *Polymer* **2020**, *12*, 1005; doi:10.3390/polym12051005.
- [3] a) H. Olivier-Bourbigou, A. Forestière, L. Saussine, L. Magna, F. Favre, F. Hugues, *Oil Gas-Eur. Magazine* **2010**, *36*, 97–102; b) D. S. McGuinness, *Chem. Rev.* **2011**, *111*, 2321–2341; c) T. Agapie, *Coord. Chem. Rev.* **2011**, *255*, 861–880; d) P. W. N. M. van Leeuwen, N. D. Clément, M. J.-L. Tschan, *Coord. Chem. Rev.* **2011**, *255*, 1499–1517; e) P.-A. Breuil, L. Magna, H. Olivier-Bourbigou, *Catal. Lett.* **2015**, *145*, 173–192; f) H. Olivier-Bourbigou, P. A. R. Breuil, L. Magna, T. Michel, M. Fernandez Espada Pastor, D. Delcroix, *Chem. Rev.* **2020**, *120*, 15, 7919–7983; g) J. Skupinska *Chem. Rev.* **1991**, *91*, 613–648.

- [4] a) S. Muthukumar Pillai, M. Ravindranathan, S. Sivaram, *Chem. Rev.* **1986**, *86*, 353–399; b) A. M. Al-Jarallah, J. A. Anabtawi, M. A. B. Siddiqui, A. M. Aitani, A. W. Al-Sa'doun, *Catal. Today* **1992**, *14*, 1–121; c) A. W. Al-Sa'doun, *Appl. Catal. A* **1993**, *105*, 1–40; d) A. Forestière, H. Olivier-Bourbigou, L. Saussine, *Oil Gas Sci. Technol.* **2009**, *64*, 649–667.
- [5] a) B. Hessen, P. J. W. Deckers, J. H. Teuben, *Angew. Chem. Int. Ed.*, **2001**, *40*, 2516–2519; b) Y. Suzuki, S. Kinoshita, A. Shibahara, S. Ishii, K. Kawamura, Y. Inoue, T. Fujita, *Organometallics*, **2010**, *29*, 2394–2396.
- [6] K. Ziegler, H. Martin, US2943125, **1960**.
- [7] N. Le Quan, D. Cruyelinck, D. Commenge, Y. Chauvin, G. Leger, *IFP Energies nouvelles* EP0135441B1, **1985**; b) D. Commenge, Y. Chauvin, J. Gaillard, J. Léonard, J. Andrews, *Hydrocarbon Process.* **1984**, *63*, 118–120.
- [8] S. M. Pillai, G. L. Tembe, M. Ravindranathan, S. Sivaram, *Ind. Eng. Chem. Res.* **1988**, *27*, 1971–1977.
- [9] a) J.-B. Cazaux, P. Braunstein, L. Magna, L. Saussine, H. Olivier-Bourbigou, *Eur. J. Inorg. Chem.* **2009**, 2942–2950; b) F. Grasset, J.-B. Cazaux, L. Magna, P. Braunstein, H. Olivier-Bourbigou *Dalton Trans.* **2012**, *41*, 10396–10404.
- [10] a) D. C. Bradley, R. C. Mehrotra, I. P. Rothwell, A. Singh, *Alkoxo and Aryloxo derivatives of metals*, Academic Press: **2001**; b) F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc. Perkin Trans.* **1987**, *2*, S1; and references cited therein c) W. Spaether, K. Klass, G. Erker, F. Zippel, R. Fröhlich, *Chem. Eur. J.* **1998**, *4*, 1411–1417; d) C. Mattheis, P. Braunstein, A. Fischer, *J. Chem. Soc. Dalton Trans.* **2001**, 800–805; e) K. Kunz, G. Erker, G. Kehr, R. Fröhlich, H. Jacobsen, H. Berke, O. Blacque, *J. Am. Chem. Soc.* **2002**, *124*, 3316–3326.
- [11] A. W. G. Platt, P. G. Pringle, *J. Chem. Soc. Dalton Trans.* **1989**, 1193–1196.
- [12] N. W. Alcock, A. W. G. Platt, P. Pringle, *J. Chem. Soc. Dalton Trans.* **1987**, 2273–2280.
- [13] N. Y. Turova, E. P. Turevskaya, V. G. Kessler, M. I. Yanovskaya, *The Chemistry of Metal Alkoxides*, Kluwer Academic Publ., Dordrecht, **2002**.
- [14] P. J. Aragon, F. Carrillo-Hermosilla, E. Villaseñor, A. Otero, A. Antiñolo, A. M. Rodríguez, *Eur. J. Inorg. Chem.* **2006**, 965–971.
- [15] T. J. Boyle, R. M. Sewell, L. A. M. Ottley, H. D. Pratt, C. J. Quintana, S. D. Bunge, *Inorg. Chem.* **2007**, *46*, 1825–1835.
- [16] S. O. Baumann, M. Bendova, M. Puchberger, U. Schubert, *Eur. J. Inorg. Chem.* **2011**, 573–580.
- [17] U. Schubert, *Acc. Chem. Res.* **2007**, *40*, 730–737.
- [18] a) P. Braunstein, F. Naud, *Angew. Chem. Int. Ed.* **2001**, *40*, 680–699; *Angew. Chem.* **2001**, *113*, 702–722; b) W.-H. Zhang, S. W. Chien, T. S. A. Hor, *Coord. Chem. Rev.* **2011**, 255, 1991.
- [19] C. L. Thurner, M. Barz, M. Spiegler, W. R. Thiel, *J. Organomet. Chem.* **1997**, *541*, 39–49.
- [20] D. J. Brauer, M. Hingst, K. W. Kottsieper, C. Liek, T. Nickel, M. Tepper, O. Stelzer, W. S. Sheldrick, *J. Organomet. Chem.* **2002**, *645*, 14–26.
- [21] a) D. L. Massart, B. G. M. Vandeginste, L. M. C. Buydens, S. de Jong, P. J. Lewi, J. Smeyers-Verbeke, *Handbook of Chemometrics and Qualimetrics, Part A*, Elsevier, Amsterdam, **1997**, pp. 643–658 and 701–737; b) E. W. Kirchhoff, D. R. Anderson, S. Zhang, C. S. Cassidy, M. T. Flavin, *Org. Process Res. Dev.* **2001**, *5*, 50–53; c) M. Marchetti, M. E. Guersoni, *Cerevisia Biotechnol.*, **1991**, *16*, 24–33; d) R. H. Myers, D. C. Montgomery, C. M. Anderson-Cook *Response Surface Methodology: Process and Product Optimization Using Designed Experiments*, Wiley Series in Probability and Statistics, **2009**.
- [22] a) R. L. J. Coetzee, D. H. Morgan, H. Maumela, *J. Appl. Stat.* **2008**, *35*, 131–147; b) Z. R. Lazic, *Design of experiments in chemical engineering*, 1st ed.; Wiley-VCH: Weinheim, **2004**; c) G. Sado, M.-C. Sado, *Les plans d'expériences, de l'expérimentation à l'assurance qualité*, AFNOR: Paris, **1991**; d) S. Corthals, T. Witvrouwen, P. Jacobs, B. Sels, *Catal. Today* **2011**, *159*, 12–24.
- [23] G. M. Sheldrick, "SHELXS-97 and SHELXL-97, Program for Crystal Structure Solution and Refinement," University of Göttingen, Göttingen, **1997**.
- [24] a) S. L. Latesky, A. K. McMullen, I. P. Rothwell, J. C. Huffman, *J. Am. Chem. Soc.* **1985**, *107*, 5981–5987; b) Y. Pérez, I. Del Hierro, I. Sierra, P. Gomez-Sal, M. Fajardo, A. Otero, *J. Organomet. Chem.* **2006**, *691*, 3053–3059.
- [25] L. J. Boehr, O. V. Dolomanov, R. J. Gildea, J. A. K. Howard, H. Puschmann, *Acta Crystallogr.* **2015**, *A71*, 59–75.



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### Titanium Complexes with Functional Alkoxido Ligands for Selective Ethylene Dimerization – A High Throughput Experimental Approach

Winning Ti! A combined High Throughput Screening (HTS) / Design of Experiment (DoE) approach, applied to functionalized alkoxido titanium complexes  $[\text{Ti}(\text{OR})_2(\text{O}i\text{Pr})_2]$ ,

allowed to identify a very active and selective Ti-based catalyst for ethylene dimerization ( $13000 \text{ g}_{\text{Ti}}^{-1} \text{ h}^{-1}$ , 93 % 1-butene) (30 bar  $\text{C}_2\text{H}_4$ ,  $55^\circ\text{C}$ , co-catalyst  $\text{AlEt}_3$ ).