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asymmetric synthesis.^[1] Complexation of organic compounds having this group with transition metals may lead to the development of unique synthetic transformations,^[2] but an olefin complex such as the one in Scheme 1 $(M = metal)^{[3]}$ has not been investigated. We report here that titanation of alkenyloxazolines proceeds nicely to give novel olefin-titanium complexes (Scheme 1, $M = Ti(OiPr)_2$), which subsequently allow for a diastereoselective multicomponent coupling process and an asymmetric coupling reaction.



Scheme 1. Generation of the olefin-metal complex.

Treatment of alkenyloxazoline $2^{[4]}$ with a titanium(II) alkoxide reagent 1 formed from $Ti(OiPr)_4$ with two equivalents of *i*PrMgCl,^[5] generates olefin complex 3,^[6] which underwent a coupling reaction with 1-octyne (4) to give titanacycle 6 ($R = C_6 H_{13}$; Scheme 2). Intermediates 3 and 6 were identified by deuteriolysis.^[7] The carbon-titanium bond α to the oxazoline (rather than the vinyl-titanium bond) of **6** selectively reacted with the octanal to give, after hydrolytic

(0.8 equiv)

–20 °C, 2–4 h R = C₆H₁₃ 4 SiMe₃ 5

SiMe₃

d.r.^[b]

Asymmetric Synthesis

Stereoselective Construction of Acyclic **Carbon Chains by a One-Pot Coupling** Process Based on Alkenyloxazoline-**Titanium Complexes****

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Oxazoline is known as a versatile functional group in organic synthesis for the activation of substrates and for

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- Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.



Ti(O/Pr)

P٢

2

2 PrMaC

Et₂O

olefinic bond. Surprisingly, the crude reaction mixture contained this adduct 8 together with a very small amount of one of the four possible diastereoisomers (d.r. = 96:4) arising from the three consecutive stereogenic centers. Compound 8 could be readily separated from this minor isomer^[8] by flash chromatography on silica gel to give a pure sample in 66% yield. The stereochemistry of 8 was determined (as depicted) by derivatization.^[7] A stereochemical course from 2 to 8 is proposed in the Supporting Information.^[7] Analogously, the sequential treatment of 2 with silvlacetylene 5 and nonanal afforded the adduct **9** in good yield. In place of the simple hydrolysis, deuteriolysis or iodinolysis of the remaining vinyltitanium bond in the intermediate **7** ($\mathbf{R} = \text{SiMe}_3$) gave deuterium-labeled and iodinated products **10** and **11**, respectively. Thus, the four-component coupling of the unsaturated oxazoline, acetylene, aldehyde, and an electrophile proceeded in one pot with nearly complete regio-, olefinic stereo-, and diastereoselectivities to give an acyclic carbon chain of the defined structure.^[9] This and the following transformations were made possible by the collaboration of the aforementioned feature of oxazolines and the behavior of the olefin–metal complex.

More results regarding the transformation of Scheme 2 are summarized in Table 1. The combination of oxazoline 2, acetylene 4 or 5, and a variety of aldehydes always showed

Table 1: Diastereoselective coupling reaction of oxazolines, acetylenes, and aldehydes according to Scheme 2.



Entry	Oxazoline		Acetylene		Aldehyde		Product	
	R ¹		R ²		R ³		Yield [%] ^[a]	d.r. ^[b]
1	Ph	2	C ₆ H ₁₃	4	C ₈ H ₁₇	8	66	96:4
2	Ph	2	C_6H_{13}	4	(E)-C ₅ H ₁₁ CH=CH-	15	54	88:12
3	Ph	2	$C_{6}H_{13}$	4	Ph	16	68	92:8
4	Ph	2	SiMe₃	5	C ₈ H ₁₇	9	73	93:7
5	Ph	2	SiMe ₃	5	iPr	17	72	90:10
6	Ph	2	SiMe ₃	5	Ph	18	70	95:5
7	p-ClC ₆ H ₄	12	SiMe ₃	5	C ₈ H ₁₇	20	62	96:4
8	1-C ₁₀ H ₇ ^[c]	13	SiMe ₃	5	C ₈ H ₁₇	21	60	95:5
9	SiMe ₃	14	SiMe ₃	5	C ₈ H ₁₇	8	48	89:11

[a] Yield of the isolated pure major isomer after chromatographic separation on silica gel. [b] Diastereoselectivity of a crude sample. Two stereoisomers were detected in the crude reaction mixture. [c] 1-Naphthyl.

high diastereoselectivities (entries 1–6). The structure of product **18** (entry 6) was also confirmed by X-ray crystallographic analysis.^[7,10] The aryl-substituted vinyloxazolines **12** and **13** also participated in the reaction (entries 7 and 8). Entry 9 illustrates the diastereoselective preparation of functionalized allylsilane **21**^[11] from (silylvinyl)oxazoline **14**.^[12]

While all reactions described above started with *E*-alkenyloxazolines, *Z*-alkenyloxazolines such as $22^{[13]}$ in Scheme 3 gave the same product 9 previously obtained from the *E*-oxazoline 2 (see Scheme 2). Rapid isomerization of the initially formed olefin complex 23 to less sterically congested 3 via the azatitanacyclopentene 24 should account for this phenomenon. The *E*-olefinic oxazolines are more readily avail-



Scheme 3. Stereochemistry of the starting alkenyloxazoline.

able than the Z isomers, and hence the former are, synthetically, the substrates of choice.

Oxazoline is a potential chiral auxiliary, $^{\left[1\right] }$ so we next

pursued the possibility of an asymmetric coupling reaction between the oxazoline-titanium complex and acetylene (Table 2). Oxazolines 25–27^[4] (R = Et, tBu, and iPr groups, respectively) were used in the reaction (entries 1-3) to evaluate the chiral induction by the oxazoline substituent R. Of these substrates, oxazoline 27 (R = iPr) prepared from (S)-valinol showed most satisfactory the result (entry 3). High chiral induction of 92:8-96:4 was uniformly observed with the valinol-derived oxazolines 27-30 to give coupling products 34-38 in good yields (entries 4-8).^[14] The stereochemistry of the products 31 and 33 was unambiguously determined as depicted by derivatization to a known compound.^[7] Optically active allylsilane **38**^[11] was easily prepared

Table 2: Asymmetric induction in the coupling of chiral oxazolines and acetylenes.



Entry		Oxazoline	ne Acetylene				Product	
	R	R ¹		R ²			Yield $[\%]^{[a]}$	d.r. ^[b]
1	Et	Ph	25	C_6H_{13}	4	31	65	75:25 ^[b,c]
2	<i>t</i> Bu	Ph	26	C ₆ H ₁₃	4	32	52	92:8 ^[d]
3	iPr	Ph	27	C_6H_{13}	4	33	72	93:7 ^[b]
4	iPr	Ph	27	SiMe ₃	5	34	73	92:8 ^[b,d]
5	iPr	p-ClC ₆ H ₄	28	C ₆ H ₁₃	4	35	67	96:4 ^[d]
6	iPr	p-ClC ₆ H ₄	28	SiMe ₃	5	36	74	94:6 ^[d]
7	iPr	1-C ₁₀ H ₇ ^[e]	29	SiMe ₃	5	37	54	95:5 ^[d]
8	iPr	SiMe ₃	30	SiMe ₃	5	38	63	95:5 ^[d]

[[]a] Yield of isolated product. [b] Enantioselectivity of the carboxylic acid produced after hydrolysis of the oxazoline. [c] In practice, the antipode of **25** was used. [d] Diastereoselectivity of a crude sample. [e] 1-Naphthyl.

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from (silylvinyl) ∞ azoline **30** with a high chiral induction (entry 8).

The oxazoline moiety of the above products should be useful for further transformations.^[1] For example, hydrolysis of **34** with dilute aqueous acid effected concomitant desilylation (Scheme 4) to give a 3-aryl-4-pentenoic acid **39**, which is a known precursor for the synthesis of neurokinin receptor antagonists.^[15]



Scheme 4. Synthetic application.

In conclusion, the novel alkenyloxazoline–titanium complexes proved to be a versatile template for diastereoselective and asymmetric coupling reactions. Further investigation on the utility of these functionalized olefin–titanium complexes and the synthetic application of the products obtained here is in progress.

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