Nozaki−Hiyama−Kishi Reactions Catalytic in Chromium

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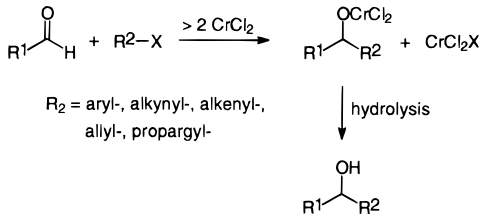
Abstract: A procedure is described which allows for the first time to perform chromium-*catalyzed* additions of organic halides to aldehydes ("Nozaki−Hiyama−Kishi reactions"). The reactions are mediated by trimethylchlorosilane, and the active Cr^{2+} species is constantly recycled by means of nontoxic, commercial manganese powder as the stoichiometric reductant. This method nicely applies to different substituted aryl, heteroaryl, alkynyl, alkenyl, and allyl halides as well as to alkenyl triflates as the starting materials and rivals its stoichiometric precedent in terms of efficiency, practicability, and chemo- and diastereoselectivity. Specifically, it has been demonstrated that the addition of crotyl bromide to various aldehydes is highly stereoconvergent, i.e. the respective *anti*-configurated homoallyl alcohols are obtained with excellent diastereomeric excess independent of whether the starting halide is (*E*)- or (*Z*)-configurated. In accordance with the likely catalytic cycle, both $CrCl_2$(cat.) or $CrCl_3$(cat) turned out to efficiently mediate reactions of this type, with the latter being preferred for practical reasons. Finally, attempts were made to optimize the number of turnovers in chromium. In this context the use of either chromocene (Cp_2Cr) or $CpCrCl_2$·THF as "pre-catalysts" were found to significantly upgrade the efficiency of such C−C bond formations, with ≤1 mol % of chromium being required in these cases for quantitative conversions.

Introduction

Since the late 1970s, Nozaki, Hiyama, and co-workers have pioneered the use of organochromium reagents in organic synthesis. In a series of seminal papers they have demonstrated that the addition of organic halides to carbonyl compounds in a "one-pot" Barbier-type fashion is efficiently and conveniently mediated by anhydrous $CrCl_2$, which either can be purchased or may be prepared from $CrCl_3$ and different reducing agents (Scheme 1).[1,2] Later on, the independent and almost simultaneous discovery made by Kishi and Nozaki that nickel salts exhibit a catalytic effect on the formation of the C−Cr bond has greatly improved the reliablity of such transformations.[3,4] These findings were far beyond the scope of earlier investigations on Cr^{2+} salts as reagents in organic synthesis[5] and have triggered extensive followup work of many other research groups.

Scheme 1



"Nozaki−Hiyama−Kishi reactions" combine some rather unique features. As far as the electrophile is concerned, they are highly aldehyde-selective. With regard to the nucleophile, however, a wide range of substrates including allyl, propargyl, alkenyl, alkynyl, and aryl halides, alkenyl triflates, and allyl sulfonates and phosphates were found to be suitable precursors for the formation of organochromium intermediates.[1,4,6−10] Most importantly, however, chromium-induced processes are distinguished by an unparalleled compatibility with an

[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1996.

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(8) (a) Jubert, C.; Nowotny, S.; Kornemann, D.; Antes, I.; Tucker, C. E.; Knochel, P. *J. Org. Chem*. **1992**, *57*, 6384−6386. (b) Knochel, P; Chou, T. S.; Jubert, C.; Rajagopal, D. *J. Org. Chem*. **1993**, *58*, 588−599. (c) Nowotny, S.; Tucker, C. E.; Jubert, C.; Knochel, P. *J. Org. Chem*. **1995**, *60*, 2762−2772.

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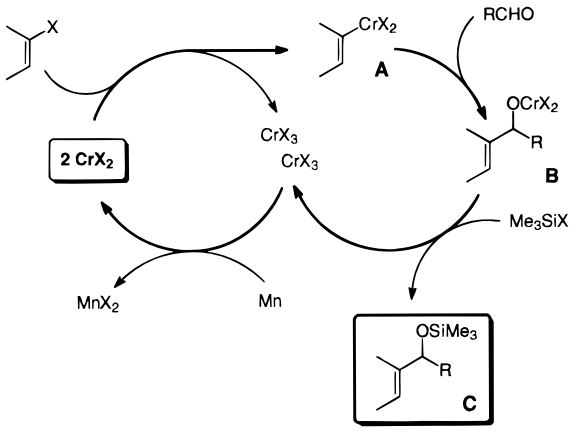
array of functional groups in *both* reaction partners. This striking chemoselectivity is nicely supplemented by some favorable stereochemical characteristics: specifically, γ-monosubstituted allylchromium reagents in general lead to the corresponding homoallyl alcohols with excellent *anti* selectivity, independent of whether the starting halide is (*E*)- or (*Z*)-configurated.[1d,6] Finally it should be noted that alkenyl halides or triflates react with complete retention of their double bond geometry.[4]

It is obvious that this unique profile renders Nozaki−Hiyama−Kishi reactions particularly well suited for applications to natural product chemistry. In fact, chromium-induced inter- or intramolecular C−C bond formations are frequently encountered as key steps in highly impressive total syntheses of target molecules of utmost complexity.[11]

Despite of these favorable distinctions, some major drawbacks must also be taken into account. Cr^{2+} is a one-electron donor; therefore, 2 mol of this reagent/mol of halide are required for the formation of an organochromium nucleophile; in practice a huge excess must be employed which is usually in the range of 400−1600 mol %, but examples with up to 100 equiv (!) of Cr^{2+} have been reported. Since chromium as well as nickel salts are physiologically highly suspicious, this precludes any application of such transformations to industrial processes. Furthermore, the rather high cost of $CrCl_2$ makes large-scale syntheses less attractive. Finally, a practical way to control the configuration of the newly formed chiral center(s) will hardly emerge from appropriate chiral ligands to chromium, if they must be used in (over)stoichiometric amounts. An efficient enantioselective version of the Nozaki−Hiyama−Kishi reaction—although highly desirable—is still missing.[12]

Scheme 2



We now report a method which allows for the first time, the Nozaki−Hiyama−Kishi reactions to be performed catalytic in chromium, without compromising the scope, practicability, efficiency, and chemo- and diastereoselectivity of such C−C bond formations.[13] As will be outlined below, a multicomponent redox system accounts for this advancement, which may help to pave the way for further applications of this valuable synthetic transformation.

Results and Discussion

Screenings and the Likely Catalytic Cycle. In the first step of a Nozaki reaction the organic halide reacts with 2 $CrCl_2$, giving rise to the desired organochromium species **A** and 1 equiv of CrX_3. The nucleophile then adds to the aldehyde with formation of the chromium alkoxide **B**. The high stability of its O−Cr^{3+} bond serves as the thermodynamic sink which drives the conversion but obviously impedes catalysis.

We reasoned that it should be possible to run Nozaki reactions catalytic in chromium if a ligand exchange between **B** and an appropriate additive can be achieved (Scheme 2): for instance, the renitent chromium alkoxide might be forced to react with an admixed chlorosilane in view of the pronounced oxophilicity of silicon. Such a σ-bond metathesis would afford the silyl ether of the desired product (**C**) and liberate the second mole of CrX_3. Since it is well precedented that Cr^{3+} salts can be reduced to Cr^{2+} by different reducing agents,[1,14] a catalytic cycle might emerge. This *overall* scenario is depicted in Scheme 2. However, it should be emphasized that this representation does not imply that each single step exactly follows the rational outlined above, but it merely serves as a working hypothesis awaiting further investigations.

In any case the choice of the stoichiometric reducing agent is decisive. It must be able to efficiently reduce CrX_3 but has to be inert toward the reducible substrates. Moreover, its salts should be significantly less toxic than those of chromium. Our previous work on low-valent titanium chemistry has suggested the use of Zn/TMSCl for such a purpose.[15] This particular reagent combination, however, has been rapidly ruled out mainly for two reasons: first, it is well-known that Zn is activated by chlorosilanes:[16] as it may then insert on its own into reactive substrates such as allyl halides, etc., one would leave the desired chromium path. Secondly and more seriously, the ZnX_2 salt

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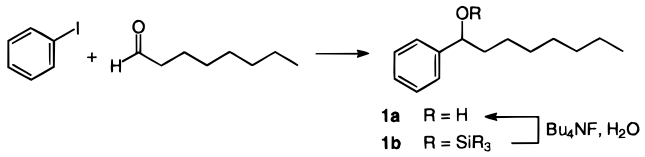
Table 1. Control Experiments: Cr^{2+}-Mediated Reaction of Iodobenzene with Octanal[a]



entry	$CrCl_2$ (mol %)	additives	T (°C)	isolated yield **1a** (%)[b]
1	400		20	78[c]
2	400		50	65
3	30	Zn, TMSCl	70	30−40[d]
4	**15**	**Mn, TMSCl**	**50**	**67**
5	**15**	**Mn, $ClMe_2Si(CH_2)_3CN$**	**50**	**72**
6	9	Mn, $ClMe_2Si(CH_2)_3CN$	50	58
7	0	Mn, $ClMe_2Si(CH_2)_3CN$	50	0[e]
8	0	Mn, $ClMe_2Si(CH_2)_3CN$, $NiCl_2$(cat.)	50	0[e]

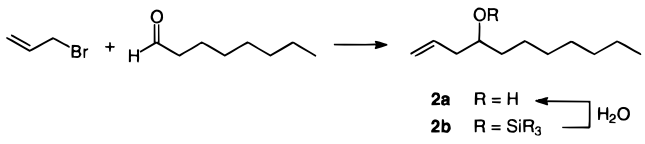
[a] The reactions were carried out in DME/DMF (20/3) unless stated otherwise, using $CrCl_2$ doped with $NiCl_2$ (∼15%). [b] After desilylation of the admixed **1b**. [c] In pure DMF. [d] Formation of 1-[(trimethylsilyl)oxy]-1-octene as side reaction; *cf.* text. [e] GC yield < 3%.

accumulating during the course of the reaction is sufficiently Lewis acidic to convert enolizable aldehydes into the corresponding silyl enol ethers in the presence of TMSCl. Because they cannot react with an intermediate organochromium species any more, the yield of the desired product will be unacceptably low. Our experiments have fully confirmed this assumption: although some turnovers could by reached in the reaction of iodobenzene with octanal using $CrCl_2$(cat.)/Zn/TMSCl, compound **1a** was obtained in rather poor yield (Table 1, entry 3). Careful GC analysis showed that 1-[(trimethylsilyl)oxy]-1-octene was in fact the major product.

A likely substitute for zinc is manganese. This metal is very cheap, its salts are essentially nontoxic, the Lewis acidity of Mn^{2+} is significantly lower than that of Zn^{2+}, and the electrochemical data hold the promise that it will form an effective redox couple with Cr^{3+}.[17] Particular mention should be made of the fact that the oxidative insertion of Mn into organic halides is largely unknown: commercial Mn powder reacts only with the most reactive substrates under special conditions.[18,19] This low intrinsic reactivity of metallic Mn toward organic molecules turned out to be the key for success in the context of the present study.

As can be seen from Tables 1 and 2, commercial Mn in combination with TMSCl and catalytic amounts of $CrCl_2$ allowed the first Nozaki−Hiyama−Kishi reactions catalytic in chromium to be performed. The control experiments clearly denote that it is the chromium salt rather than the Mn(0) which accounts for the results obtained: neither Mn/R_3SiCl nor Mn/R_3SiCl/$NiCl_2$(cat) lead to any product formation in the reaction of iodobenzene and octanal (GC < 3%) (Table 1, entries 7 and 8). The same holds true for the reaction of allyl bromide with octanal, where only a tiny amount of product is detected in GC after extended periods of time (90 h) if the reaction is carried out in the absence of chromium salts (Table 2, entry 3). In clear contrast, however, *a combination of catalytic amounts of $CrCl_2$, Mn powder, and a chlorosilane rapidly and cleanly converts these substrates into the desired products.* They are isolated after a final aqueous workup (in the presence of *n*-Bu_4NF for the more stable silyl ethers) which ensures the desilylation of the crude product mixture. The yields thus obtained favorably compare to those of the control experiments employing overstoichiometric amounts of $CrCl_2$.

Table 2. Control Experiments: Cr^{2+}-Mediated Reaction of Allyl Bromide with Octanal[a]



entry	$CrCl_2$ (mol %)	additives	T (°C)	isolated yield (%)[b]
1	400		rt	81
2	7	Mn, TMSCl	rt	78
3	0	Mn, TMSCl	rt	<19 (GC)[c]

[a] All reactions were carried out with undoped $CrCl_2$ in THF; reaction time 6 h. [b] Refers to the yield of the unprotected alcohol **2a** obtained after desilylation of the crude product. [c] After 90 h reaction time.

Gratifyingly, this catalytic procedure applies to all important kinds of substrates known to undergo Nozaki−Hiyama−Kishi reactions. The chemo- and diastereoselectivities observed in these chromium-catalyzed processes perfectly match those reported for the stoichiometric set-up. The experience gained during our study is summarized below.

Cr-Catalyzed Reactions of Aryl and Alkenyl Halides and Triflates. For an efficient conversion these substrates require ∼15 mol % of $CrCl_2$ which must additionally be doped with $NiCl_2$. The $CrCl_2$ used should be colorless; pale-green batches result in lower yields. Reasonable reaction rates are achieved at 50(±3) °C. A mixture of DME/DMF (20/3) turned out to be the best solvent, although pure DMF was found superior in the stoichiometric process. The DMF used as the cosolvent must be thoroughly purified in order to ensure reproducible results; for details see the Experimental Section.

Although very few examples of stoichiometric Nozaki−Hiyama−Kishi reactions with aryl halides have been reported so far,[1c] we find that our catalytic procedure nicely applies to this group of substrates. As can be seen from the results compiled in Table 3, iodobenzene reacts readily with aromatic as well as with different aliphatic aldehydes in the presence of $CrCl_2$(cat.)/Mn/chlorosilane. Entry 4 shows that the presence of an alkyl chloride in the electrophile does not intervene at all. Similarly, the reaction turned out to be compatible with an

(15) The combination of $TiCl_3$(cat.), Zn, and R_3SiCl accounts for the first carbonyl-coupling reactions catalytic in titanium; *cf.*, (a) Fürstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468−4475. For related work on stoichiometric reactions with $TiCl_3$/Zn, see: (b) Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215−5229. (c) Fürstner, A.; Ptock, A.; Weintritt, H.; Goddard, R.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 678−681. (d) Fürstner, A.; Weintritt, H.; Hupperts, A. *J. Org. Chem.* **1995**, *60*, 6637−6641. (e) Fürstner, A.; Ernst, A. *Tetrahedron* **1995**, *51*, 773−786. (f) Fürstner, A.; Ernst, A.; Krause, H.; Ptock, A. *Tetrahedron* **1996**, *52*, 7329−7344. (g) Review: Fürstner, A.; Bogdanovic, B. *Angew. Chem.* **1996**, *108*, 2583.

(16) (a) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390−2392. For a timely review see: (b) Knochel, P. in *Active Metals. Preparation, Characterization, Applications*; Fürstner, A.; Ed.; VCH: Weinheim, 1996; pp 191−236.

(17) Electrochemical redox potentials: $Cr^{3+} + e^- \rightleftharpoons Cr^{2+}$ (−0.41 V); $Zn^{2+} + 2e^- \rightleftharpoons Zn$ (−0.76 V); $Mn^{2+} + 2e^- \rightleftharpoons Mn$ (−0.3 V); *cf.*; *Handbook of Chemistry and Physics*; 2nd ed.; CRC press: Boca Raton, FL, 1982.

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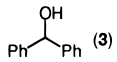
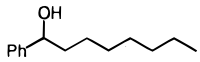
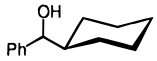
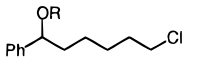
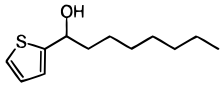
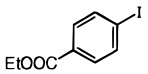
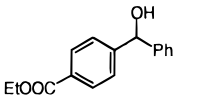
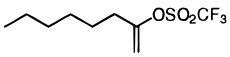
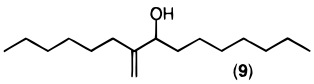
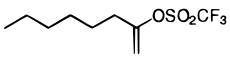
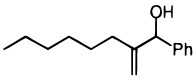
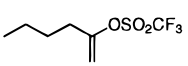
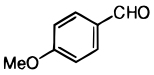
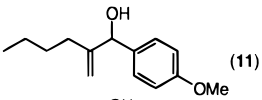
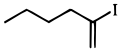
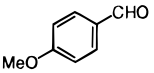
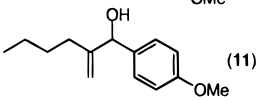
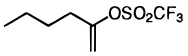
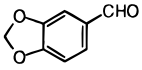
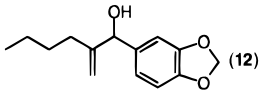
(19) However, highly activated Mn powder prepared by reduction of manganese salts with either lithium naphthalenide (a) or potassium graphite laminate (b) is capable to insert into different kinds of organic halides; *cf.*: (a) Kim, S. H.; Hanson, M. V.; Rieke, R. D. *Tetrahedron Lett.* **1996**, *37*, 2197−2200. (b) Fürstner, A.; Brunner, H., *Tetrahedron Lett.* **1996**, *37*, 7009−7012. This latter paper demonstrates that the addition of crotylmanganese bromide to aldehydes is diastereodivergent and results in much lower diastereoselectivity as compared to crotylchromium halide additions. See also: (c) Hiyama, T.; Obayashi, M.; Nakamura, A. *Organometallics* **1982**, *1*, 1249−1251.

Table 3. Chromium-Catalyzed Reactions of Aryl Iodides, Alkenyl Iodides, and Alkenyl Triflates with Different Aldehydes[a]

Entry	R-X	Aldehyde	Product	$ClMe_2Si(CH_2)_3CN$ Yield (%)[b]	Me_3SiCl Yield (%)[b]
1	PhI	PhCHO	 (**3**)	88	62
2	PhI	$CH_3(CH_2)_6CHO$	 (**1a**)	72	67
3	PhI	$C_6H_{11}CHO$	 (**4**)	71	
4	PhI	$Cl(CH_2)_5CHO$	 (**5**) R = Ac (**6**) R = H		66[c]
5		$CH_3(CH_2)_6CHO$	 (**7**)	57	
6		PhCHO	 (**8**)		57[d]
7		$CH_3(CH_2)_6CHO$	 (**9**)		61
8		PhCHO	 (**10**)		67
9			 (**11**)		76
10			 (**11**)		75
11			 (**12**)		80

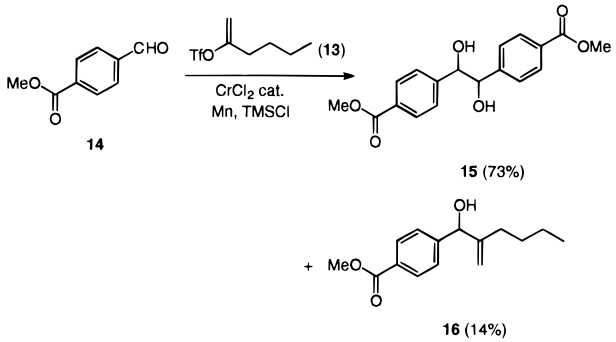
[a] All reactions were carried out with $CrCl_2$ (15 mol %, doped with $NiCl_2$ cat.), Mn powder (4.2 mmol), aldehyde (2.5 mmol), R-X (5 mmol), chlorosilane (6 mmol) in DMF/DME (20/3) at 50 °C. [b] Refers to the product obtained after desilylation (aqueous Bu_4NF) of the crude mixture. [c] Isolated as the *O*-acetate after acetylation of the crude product. [d] 4,4′-Bis(ethoxycarbonyl)diphenyl as byproduct (20% based on $I\text{-}C_6H_4COOEt$).

ester group in the nucleophile (entry 6) and can be extented to heteroaromatic compounds such as 2-iodothiophene (entry 5).

Likewise, alkenyl iodides and alkenyl triflates[4,20] reacted smoothly under our standard conditions. However, we noticed a subtle influence of the electronic properties of the chosen aldehyde on the reaction path which has not yet been reported in the literature. While aliphatic aldehydes, benzaldehyde, and analogues bearing electron-donating substituents such as an alkoxy or an acetal group behaved properly leading to the expected allyl alcohols in good to excellent yields (Table 3, entries 7−11), some deviation from the known reaction path was observed with methyl 4-formylbenzoate (**14**) as the substrate (Scheme 3).

Although the ester function *per se* is compatible, its electron-withdrawing character obviously facilitates a single-electron transfer from the low-valent metal salt to the aldehyde group of **14**. As a consequence, the oxidative insertion of Cr^{2+} into the alkenyl triflate **13** has to compete with the formation of the ketyl radical which undergoes a subsequent pinacol coupling leading to diol **15** as the major product. However, this observation is in line with previous experiences gathered in reductive carbonyl coupling reactions which proceed particularly well with electron-poor arylaldehydes as the substrates.[21,22]

Scheme 3



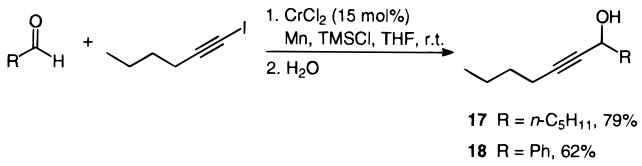
Some screenings have been performed to see if the turnover number of the chromium salt may be improved by replacing TMSCl by other additives. As can be seen from the data included in Tables 1 and 3, the use of $ClMe_2Si(CH_2)_3CN$ did not significantly upgrade the results, although this particular additive had recently turned out superior in the context of oxo

(20) Takai, K.; Sakogawa, K.; Kataoka, Y.; Oshima, K.; Utimoto, K. *Org. Synth.* **1993**, *72*, 180−188.

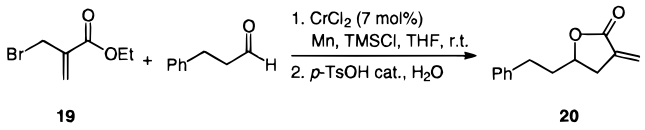
(21) Fürstner, A.; Csuk, R.; Rohrer, C.; Weidmann, H. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1729−1734 and lit. cit.

(22) There are some scattered reports in the literature on the use of chromium salts in pinacolization reactions; *cf.*: (a) Davis, D. D.; Bigelow, W. B. *J. Am. Chem. Soc.* **1970**, *92*, 5127−5130. (b) Conant, J. B.; Cutter, H. B. *J. Am. Chem. Soc.* **1926**, *48*, 1016−1030. (c) Sopher, D. W.; Utley, J. H. P. *J. Chem. Soc., Chem. Commun.* **1979**, 1087−1088.

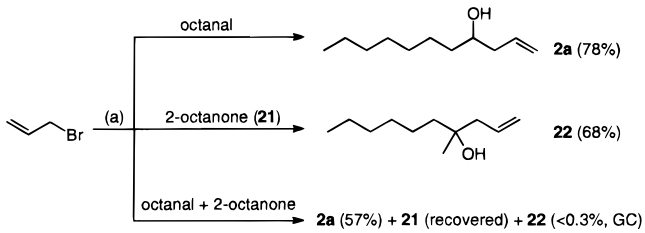
Scheme 4



Scheme 5



Scheme 6[a]



[a] Key: (a) (i) $CrCl_2$ (7 mo %), Mn, TMSCl, THF, room temperature; (ii) H_2O.

amide coupling reactions catalytic in low-valent titanium.[15] Obviously its nitrile group is too weak a ligand to chromium to exert any appreciable effect. Similarly, neither the addition of catalytic amounts of LiI to the reaction mixture nor replacing TMSCl by TMSBr, $(EtO)_3SiCl$, or $ClMe_2SiCH_2CH_2SiMe_2Cl$ resulted in better turnovers. For a more successful way to upgrade the efficiency of the catalytic process by variation of the chromium source rather than the chlorosilane additive see the final paragraph of this section.

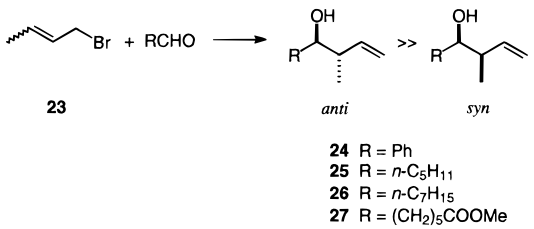
Cr-Catalyzed Reactions of Alkynyl Halides. The two examples depicted in Scheme 4 substantiate that our standard catalytic system works properly with alkynyl iodides as substrates.[1e] When performed in THF at room temperature, good yields of the corresponding propargyl alcohols **17** and **18,** respectively, can be obtained after an aqueous workup of the crude reaction mixture.

Cr-Catalyzed Reactions of Allyl Halides: Chemo- and Diastereoselectivity. When allyl halides are used as the substrates, ~7 mol % of *undoped* $CrCl_2$ turned out to be sufficient (Table 2). The presence of trace amounts of nickel salts in the chromium catalyst is detrimental because it seems to bias Wurtz-type couplings of these substrates. The reactions can be conveniently carried out at ambient temperature in THF as the preferred solvent. The use of substituted allyl halides such as ethyl 2-(bromomethyl)-2-propenoate (**19**) does not pose any problems but leads cleanly to the corresponding α-methylene γ-lactone **20** after an aqueous acidic workup (Scheme 5).[23]

It is well established that organochromium reagents in general react much more readily with aldehydes than with ketones.[1,2] The new catalytic protocol also features this clearcut chemoselectivity (Scheme 6). In fact, excellent results were obtained in the chromium-catalyzed reaction of allyl bromide with octanal, whereas 2-octanone (**21**) affords 68% isolated yield of the respective alcohol **22** under the same reaction conditions. However, if a 1:1 mixture of octanal and 2-octanone is used in order to probe the relative reaction rates, the aldehyde is attacked exclusively whereas the admixed ketone remains completely unchanged (addition to the ketone < 0.3% in GC).

(23) For the synthesis of α-methylene γ-lactones using overstoichiometric amounts of chromium salts, see: (a) Okuda, Y.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Chem. Lett*. **1985**, 481−484. (b) Mattes, H.; Benezra, C. *J. Org. Chem*. **1988**, *53*, 2732−2737.

Scheme 7



Of even greater significance is the diastereoselectivity observed in chromium-catalyzed reactions of crotyl bromides and related systems. As has been mentioned in the introduction, Nozaki−Hiyama−Kishi reactions of γ-monosubstitued allyl halides are distinguished by an excellent preference for the formation of the *anti*-configurated homoallyl alcohol regardless of whether the substrate is (*E*)- or (*Z*)-configurated (Scheme 7).[1,6,24] In contrast to this pattern of *γ-monosubstituted* allyl halides, *γ,γ-disubstituted* donors follow a stereodivergent course as has been shown in recent work of Knochel et al.[8]

The stereoselectivities observed in the reaction of a representative set of substituted allylic halides under our standard catalytic conditions are in full accordance with this literature precedence (Table 4). Specifically, the *anti*-selectivity observed in the reaction of (*E*)-crotyl bromide (*E*-**23**) with different aldehydes was reproducibly >90:10, i.e. in the same order or even better than the selectivity reported in the literature for the respective stoichiometric processes. The analogous transformations with (*Z*)-crotyl bromide (*Z*-**23**) as the substrate again led to the *anti*-configurated product in a diastereomeric ratio of dr = 90:10. This stereoconvergent behavior clearly reflects the typical characteristics of a crotyl chromium intermediate[1,6] and therefore provides an additional indication that our procedure is in fact a chromium-catalyzed rather than a manganese-induced reaction.[19b] Final support for this assumption stems from an experiment with geranyl bromide (**28**, X = Br) and benzaldehyde as the substrates: In full accord with Knochel's work,[8c] this transformation led to the (*S**,*S**)-configurated compound **29** as the major product rather than the (*S**,*R**)-diastereoisomer with a dr = 94:6 (Table 5).

Reactions Catalyzed by $CrCl_3$. If the reaction owes its performance to an efficient $Cr^{2+} \rightleftharpoons Cr^{3+}$ redox process as suggested by Scheme 2 and substantiated by the results outlined above, it should proceed no matter at which oxidation state the catalytic process is started. However, keeping the rather high cost and the air-sensitivity of $CrCl_2$ in mind, it might considerably upgrade the protocol in practical terms if $CrCl_2$ can be replaced by $CrCl_3$ as a precatalyst.

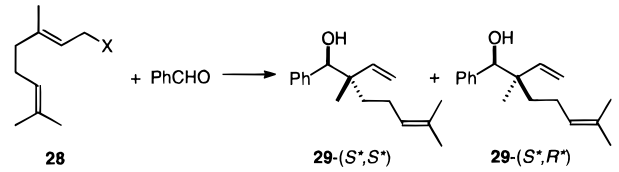
A series of experiments using crotyl bromide as the starting material has unequivocally confirmed this possibility. For comparative reasons the results obtained have been included in Table 4 (entries 4, 5, and 8). As can be seen from these data, (i) the reaction path is again diastereoconvergent, i.e. the use of (*E*)- and (*Z*)-crotyl bromide results in the same *anti*-configurated homoallyl alcohol, (ii) the diastereoselectivity perfectly matches that observed in the $CrCl_2$ cases, and finally (iii) the isolated yields are as high as or even slightly better than those obtained in the $CrCl_2$-triggered reactions. An additional example using methyl 7-oxoheptanoate as the electrophile

(24) For general reviews on reactions of crotylmetal reagents with carbonyl compounds and for a pertinent discussion on the origins of the observed diastereoselection, see: (a) Hoffmann, R. W. *Angew. Chem*. **1982**, *94*, 569−580. (b) Yamamoto, Y.; Asao, N. *Chem. Rev*. **1993**, *93*, 2207−2293.

Table 4. Chromium-Catalyzed Reactions of Crotyl Bromide with Different Aldehydes

entry	crotyl bromide	R	chromium salt	additives	product (% yield)	*anti:syn*
1	(*E*)-**23**	Ph	$CrCl_2$ (400 mol %)		**24** (100)	90:10 [1d]
2	(*E*)-**23**	Ph	$CrCl_2$ (7 mol %)	Mn, TMSCl	**24** (79)	94:6
3	(*Z*)-**23**	Ph	$CrCl_2$ (7 mol %)	Mn, TMSCl	**24** (64)	90:10
4	(*E*)-**23**	Ph	$CrCl_3$ (7 mol %)	Mn, TMSCl	**24** (85)	91:9
5	(*Z*)-**23**	Ph	$CrCl_3$ (7 mol %)	Mn, TMSCl	**24** (74)	90:10
6	(*E*)-**23**	*n*-C_5H_{11}	$CrCl_2$ (400 mol %)		**25** (97)	96:4 [1d]
7	(*E*)-**23**	*n*-C_5H_{11}	$CrCl_2$ (7 mol %)	Mn, TMSCl	**25** (84)	92:8
8	(*E*)-**23**	$(CH_2)_5COOMe$	$CrCl_3$ (7 mol %)	Mn, TMSCl	**27** (83)	92:8

Table 5. Chromium-Induced Reactions of Geranyl Substrates with Benzaldehyde: Comparision between the Catalytic and the Stoichiometric Procedures



28 **29**-(*S*,S**) **29**-(*S*,R**)

entry	X	chromium salt	additives	yield (%)	diastereomeric ratio *S*,S**:*S*,R**
1	$OP(O)(OEt)_2$	$CrCl_2$ (215 mol %)		94[a]	97:3 (ref 8c)
2	Br	$CrCl_2$ (7 mol %)	Mn, TMSCl	79[b]	94:6

[a] In DMPU as the solvent in the presence of LiI. [b] In THF as solvent.

Table 6. Nozaki−Hiyama−Kishi Reactions Catalyzed by Chromocene (Cp_2Cr) or $CpCrCl_2$·THF[a]

entry	R-X	aldehyde	chromium source	product (isolated yield, %)	dr
1	allyl bromide	octanal	Cp_2Cr (2%)	**2a** (73)	
2	allyl bromide	octanal	Cp_2Cr (1%)	**2a** (76)	
3	allyl bromide	octanal	Cp_2Cr (0.5%)	**2a** (62)	
4	(*E*)-**23**	benzaldehyde	Cp_2Cr (1%)	**24** (37)[b]	
5	(*E*)-**23**	octanal	Cp_2Cr (1%)	**26** (76)	*anti*:*syn* = 77:23
6	(*E*)-**23**	octanal	$CpCrCl_2$·THF	**26** (92)	*anti:syn* = 78:22
7	(*Z*)-**23**	octanal	Cp_2Cr (1%)	**26** (60)	*anti:syn* = 65:35
8	(*E*)-**23**	$MeOOC(CH_2)_5CHO$	Cp_2Cr (1%)	**27** (76)	*anti:syn* = 78:22
9	1-iodo-1-hexyne	hexanal	Cp_2Cr (5%)	**17** (80)	
10	1-iodo-1-hexyne	hexanal	Cp_2Cr (1%)	**17** (56)	
11	2-(triflyloxy)-1-octene	octanal	Cp_2Cr (9%)[c,d]	**9** (71)	
12	iodobenzene	octanal	Cp_2Cr (9%)[c,d]	**1a** (59)	

[a] All reactions were carried out in THF at ambient temperature unless stated otherwise. [b] Together with 56% isolated yield of the pinacolization product 1,2-diphenyl-1,2-ethanediol. [c] The chromium catalyst was additionally doped with $NiCl_2$. [d] In DME/DMF (20/3) at 50 °C.

has been included in order to verify again the compatibility of an ester group under these conditions (Table 4, entry 8).

Use of Cp_2Cr or $CpCrCl_2$·THF as Precatalysts: Improved Turnover Numbers. Aiming at a further reduction of the amount of chromium in C−C bond formations of this type, we considered the possibility of improving the turnover number of the catalyst by fine-tuning its redox potential by means of appropriate ligands. Much to our surprise, a screening of the extensive literature on Nozaki−Hiyama−Kishi reactions revealed that this possibility has hardly been considered in the context of the stoichiometric procedure. A pertinent exception is a recent publication by Wipf et al., claiming that the performance of a diphenylchromium−TMEDA complex significantly exceeds that of $CrCl_2$.[25] However, as the C−Cr bond in Ph_2Cr might not resist TMSCl in our catalytic scenario, we were looking for other chromium complexes bearing electron-donating but "dummy" ligands. An obvious choice is chromocene Cp_2Cr (Cp = cyclopentadienyl) which is easily prepared and also commercially available.[26] It is known that chromocene suffers cleavage of one of the Cp rings on treatment with allyl halides in THF or other donor solvents with formation of the respective $CpCrX_2$−solvent complex.[27] However, keeping in mind that our catalytic cycle will proceed regardless of whether we start with Cr^{2+} or Cr^{3+} (*vide supra*), the loss of one of the Cp rings should not matter; the well accessible and somewhat more stable "$CpCrCl_2$" (either in form of its dimer $[CpCrCl_2]_2$ or as the solvent complex $CpCrCl_2$·THF) may also be considered a suitable precursor for our purposes.[28]

From the results summarized in Table 6 it is obvious that the turnover number may in fact be considerably improved if $CrCl_2$ is replaced by chromium "precatalysts" bearing Cp rings. Cp_2Cr and $CpCrCl_2$·THF worked equally well: As little as ≤1 mol % of these chromium sources turned out to be sufficient in

(25) Wipf, P.; Lim, S. *J. Chem. Soc., Chem. Commun*. **1993**, 1654−1656.

(26) For a convenient preparation, see: (a) Köhler, F. H.; Prössdorf, W. *Z. Naturforsch*. **1977**, *32B*, 1026−1029. (b) *Organometallic Synthesis*; King, R. B., Ed.; Academic Press: New York, 1965; Vol. 1, pp 66−67.

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(28) $CpCrCl_2$·THF can be conveniently prepared from Cp_2Cr and HCl gas in THF at 0 °C on a large scale; *cf*.: (a) Klocke, H., Dissertation, Ruhr Universität Bochum, 1984. (b) For the preparation of the dimer $[CpCrCl_2]_2$ by the same reaction using pentane instead of THF as the solvent and for its use in the synthesis of π-allyl complexes, see: Betz, P.; Döhring, A.; Emrich, R.; Goddard, R.; Jolly, P. W.; Krüger, C.; Romao, C. C.; Schönfelder, K. U.; Tsay, Y. H. *Polyhedron* **1993**, *12*, 2651−2662 and literature cited.

reactions of allyl halides with aldehydes. This denotes a significant advancement compared with the ∼7 mol % of $CrCl_2$ (or $CrCl_3$) which are required otherwise. Similarly, a distinct although less spectacular reduction of the amount of chromium could be achieved in reactions of alkenyl triflates as well as alkynyl and aryl iodides as the substrates.

The increased performance of the CpCr-based catalytic process, however, is somewhat corroded by a slightly lower diastereoselectivity. Although the reaction of crotyl bromide again leads to the preferential formation of the *anti*-homoallyl alcohol irrespective of the double bond geometry of the starting material, the *anti*:*syn* ratio is less favorable than in the $CrCl_x$-catalyzed process ($x = 2, 3$) but remains still in a preparatively useful range (Table 6, entries 5−8). Moreover, it clearly emerged from our study that the Cp_2Cr-catalyzed method applies only to aliphatic aldehydes as substrates, while aromatic ones are prone to pinacol coupling when exposed to this more electron-rich metal template (Table 6, entry 4).[22]

Summary and Outlook. We have described the first Nozaki−Hiyama−Kishi reactions using catalytic amounts of chromium salts in combination with the cheap and nontoxic manganese as a suitable stoichiometric reductant. The process is mediated by trimethylchlorosilane and meets all criteria set by the stoichiometric precedent with regard to the scope and the chemo- and the diastereoselectivity. It has been shown that either $CrCl_2$ or $CrCl_3$ is a suitable catalyst, with the latter being preferred for practical reasons. Although the amount of chromium salt (∼7 mol % for allylic and 15 mol % for aryl and alkenyl substrates) may still seem inappropriately high for industrial applications of this method, we consider it to be an important step forward as compared to the large excess of chromium salts which are usually employed for reactions of this type. One of the limiting factors for the turnover number seems to be an incomplete ligand exchange between the chromium alkoxide initially formed and the admixed chlorosilane.[29] Finally we have gained the insight that different chromium sources catalyze reactions of this type, with CpCr-templates being particularly promising. As little as ≤1 mol % of either Cp_2Cr or $CpCrCl_2$·THF as the "pre-catalysts" in combination with Mn and TMSCl account for highly efficient C−C bond formations. This holds the promise of further improving the efficiency of the process and may help to endow the catalyst with a periphery of chiral ligands. Several options along these lines are actively being pursued in our laboratory.[30]

Experimental Section

General Procedures. All reactions were carried out under Ar using Schlenk techniques. $CrCl_2$: The $CrCl_2$ used should be colorless; pale-green batches result in lower yields. Samples of good quality were purchased from Alfa-Johnson Matthey Co. (99.9% purity). $CrCl_3$ (99%), $NiCl_2$ (98%) and Mn powder (ca. 150 μm) were purchased from Aldrich and used as received. Cp_2Cr and $CpCrCl_2$·THF were prepared according to literature procedures.[26,28] The solvents were dried by distillation over the following drying agents and were transferred under Ar: DME (Na/K alloy), THF (Na/benzophenone). The DMF must be thorougly purified; best results were obtained by distilling predried DMF over Desmodur-15 (Bayer AG) and dibutyltin laurate at 70−80 °C under reduced pressure. TMSCl (Janssen), the commercially available aldehydes, iodobenzene, iodothiophene, allyl bromide, (*E*)-crotyl bromide (*E*-**23**), geranyl bromide (**28**), and ethyl 2-(bromomethyl)-2-propenoate (**19**) were distilled prior to use. (Cyanopropyl)dimethylchlorosilane (Aldrich) was used as received. Flash chromatography: Merck silica gel 60 (230−400 mesh) with hexane/ethyl acetate in various proportions as eluent. Instrumental analyses: NMR spectra were recorded on a Bruker AC 200 spectrometer at 200.1 MHz (^{1}H) and 50.3 MHz (^{13}C) in $CDCl_3$. Chemical shifts (δ) are given in ppm relative to TMS. IR spectra were recorded on a Nicolet FT-7199, wavenumbers are in cm^{-1}. Mass spectra were recorded on a Varian CH-5 (70 eV).

Substrates. 2-[[(Trifluoromethyl)sulfonyl]oxy]-1-octene,[20] 2-[[(trifluoromethyl)sulfonyl]oxy]-1-hexene,[20] 1-iodo-1-hexyne,[31] (*Z*)-crotyl bromide (*Z*-**23**),[32] and methyl 7-oxoheptanoate[33] were prepared according to the literature procedures cited. 2-Iodo-1-hexene was obtained upon reaction of 1-hexyne with 9-iodo-9-BBN, followed by deborylation with HOAc.[34]

Representative Procedure for the $CrCl_2$-Catalyzed Reaction of Aryl and Alkenyl Halides (Triflates) with Aldehydes. 1-(4-Methoxyphenyl)-2-methylene-1-hexanol (11). A solution of 4-methoxybenzaldehyde (340 mg, 2.5 mmol), 2-[[(trifluoromethyl)sulfonyl]oxy]-1-hexene (1.06 g, 4.6 mmol) and TMSCl (0.75 mL, 6.0 mmol) in DMF (1.5 mL) and DME (5 mL) was dropped into a suspension of Mn powder (230 mg, 4.2 mmol), $CrCl_2$ (46 mg, 0.38 mmol), and $NiCl_2$ (10 mg, 0.07 mmol) in DME (5 mL) at 50 °C. After being stirred for 5 h at that temperature, the mixture was quenched with water (15 mL) and extracted with ethyl acetate (150 mL in three portions), and the combined organic layers were washed with brine. Aqueous *n*-Bu_4NF (75% w/w) was added, and the solution was stirred at room temperature until TLC showed complete desilylation of the crude product. Standard workup followed by flash chromatography with hexane/ethyl acetate (15/1) as eluent afforded the title compound as a colorless syrup (420 mg, 76%). ^{1}H NMR: δ 0.83 (t, 3H), 1.15−1.45 (m, 4H), 1.72- 2.05 (m, 2H), 2.18 (b, 1H), 3.77 (s, 3H), 4.94 (s, 1H), 5.05 (s, 1H), 5.22 (s, 1H), 6.85 (d, 2H), 7.25 (d, 2H). ^{13}C NMR: δ 13.6, 22.1, 29.6, 31.4, 54.9, 76.4, 108.7, 113.2, 127.7, 134.2, 151.0, 158.8. IR: 3410, 2957, 2931, 2871, 1630, 1611, 1511, 1465, 1249, 1172, 1036, 910, 830. MS: *m/z* (relative intensity) 220 (100, [M^+]), 177 (13), 163 (26), 137 (86), 109 (17).

The products compiled below were obtained analogously.

Diphenylmethanol (3). This compound was identified by comparison with an authentic sample (Aldrich).

1-Phenyl-1-octanol (1a). Colorless syrup. ^{1}H NMR: δ 0.92 (t, 3H), 1.31 (m, 8H), 1.79 (m, 2H), 1.97 (s, 1H), 4.69 (t, 1H), 7.37 (s, 5H). ^{13}C NMR: δ 13.7, 22.3, 25.5, 28.9, 29.2, 31.5, 38.8, 74.3, 125.6, 127.1, 128.0, 144.6. IR: 3360, 1600, 1500, 1450, 1060, 1030, 760, 700. MS: *m/z* (relative intensity) 206 (3, [M^+]), 107 (100), 79 (25), 77 (12).

Phenylcyclohexylcarbinol (4). ^{1}H NMR: δ 0.78−1.45 (m, 6H), 1.48−1.85 (m, 4H), 1.95 (b, 1H), 2.00 (s, 1H), 4.33 (d, 1H), 7.29 (m, 5H). ^{13}C NMR: δ 25.8, 26.1, 28.5, 29.0, 44.6, 79.0, 126.4, 127.0, 127.8, 143.3. IR: 3395, 3028, 2924, 2852, 1603, 1493, 1451, 1259, 1068, 1017, 893, 760, 701, 578. MS: *m/z* (relative intensity) 190 (4, [M^+]), 107 (100), 79 (28).

1-Acetoxy-6-chloro-1-phenylhexane (5). In this case the product was isolated after acetylation (Ac_2O, pyridine) of the crude reaction mixture. Colorless syrup. ^{1}H NMR: δ 1.22−1.59 (m, 4H), 1.70−2.05 (m, 4H), 2.11 (s, 3H), 3.54 (t, 2H), 5.79 (t, 1H), 7.36 (s, 5H). ^{13}C NMR: δ 20.9, 24.5, 26.2, 32.0, 35.8, 44.5, 75.5, 126.1, 127.5, 128.1, 140.3, 170.0. IR: 3065, 3033, 2941, 2863, 1737, 1495, 1455, 1372, 1239, 1073, 1024, 964, 760, 700, 650, 553. MS: *m/z* (relative intensity) 254 (6, [M^+]), 212 (34), 149 (39), 117 (35), 107 (100), 43 (84).

1-Phenyl-6-chloro-1-hexanol (6). Obtained upon deacetylation (MeOH, NaOMe(cat.)) of the acetate mentioned above. Colorless syrup. ^{1}H NMR: δ 1.21−1.54 (m, 4H), 1.62−1.91 (m, 5H), 3.50 (t, 2H), 4.66 (t, 2H), 7.33 (s, 5H). ^{13}C NMR: δ 24.7, 26.4, 32.1, 38.5, 44.6, 74.1, 125.5, 127.2, 128.1, 144.4. IR: 3374, 3029, 2937, 2860, 1603, 1493, 1454, 1310, 1282, 1201, 1028, 914, 762, 701, 650. MS: *m/z* (relative intensity) 184 (2, [M^+]), 107 (100), 79 (29).

(29) Complete silylation could not be reached. This seems to be a limiting factor for the number of turnovers.

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1-(2-Thienyl)-1-octanol (7). Colorless syrup. ^{1}H NMR: δ 0.90 (t, 3H), 1.29 (m, 10H), 1.86 (m, 2H), 2.04 (b, 1H), 4.92 (t, 1H), 6.98 (m, 3H), 7.24 (m, 2H). ^{13}C NMR: δ 13.7, 22.3, 25.4, 28.8, 29.0, 31.4, 39.0, 69.7, 123.3, 124.1, 126.2, 148.7. IR: 3377, 2955, 2927, 1465, 1415, 1378, 1231, 1039, 853, 830, 697. MS: *m/z* (relative intensity) 212 (10, [M$^+$]), 113 (100), 85 (22).

[4-(Ethoxycarbonyl)phenyl]phenylmethanol (8). Colorless syrup. ^{1}H NMR: δ 1.36 (t, 3H), 2.65 (b, 1H), 4.33 (q, 2H), 5.84 (s, 1H), 7.31 (m, 5H), 7.43 (d, 2H), 7.99 (d, 2H). ^{13}C NMR: δ 14.0, 60.6, 75.5, 125.9, 126.3, 127.5, 128.3, 129.4, 143.0, 148.3, 166.1. IR: 3461, 3062, 3030. 2982, 1716, 1700, 1611, 1453, 1413, 1368, 1279, 1176, 1106, 1019, 873, 755, 701. MS: *m/z* (relative intensity) 256 (16, [M$^+$]), 211 (14), 183 (13), 177 (30), 165 (11), 151 (100), 123 (32), 105 (63), 77 (27).

7-Methylenepentadecan-8-ol (9). Colorless syrup. ^{1}H NMR: δ 0.88 (m, 3H), 1.29−1.55 (m, 23H), 2.00 (m, 2H), 4.05 (t, 1H), 4.83 (d, 1H), 5.00 (d, 1H). ^{13}C NMR: δ 13.7, 22.3, 25.4, 27.7, 28.9, 29.2, 31.0, 31.4, 31.5, 35.2, 75.2, 108.7, 152.0. IR: 3354, 2956, 2927, 2857, 1646, 1466, 1378, 1122, 1047, 1020, 900, 724. MS: *m/z* (relative intensity) 240 (3, [M$^+$]), 169 (12), 155 (18), 141 (29), 127 (26), 123 (20), 95 (17), 81 (35) 71 (100).

2-Methylene-1-phenyl-1-octanol (10). Colorless syrup. ^{1}H NMR: δ 0.85 (t, 3H), 1.18−1.51 (m, 8H), 1.75−2.08 (m, 3H), 4.98 (s, 1H), 5.16 (s, 1H), 5.27 (s, 1H); 7.33 (m, 5H). ^{13}C NMR: δ 13.7, 22.2, 27.4, 28.7, 31.3, 31.5, 77.0, 109.3, 126.4, 127.3, 128.0, 141.9, 150.9. IR: 3376, 3029, 2956, 2928, 2858, 1647, 1493, 1454, 1038, 1026, 903, 841, 763, 699. MS: *m/z* (relative intensity) 218 (38, [M$^+$]), 147 (24), 133 (100), 129 (10), 120 (50), 107 (46), 105 (33), 91 (10), 79 (29), 77 (19), 55 (21).

2-Methylene-1-[3,4-(methylenedioxy)phenyl]-1-hexanol (12). Colorless syrup. ^{1}H NMR: δ 0.85 (t, 3H), 1.17−1.46 (m, 4H), 1.65−2.04 (m, 3H), 4.95 (s, 1H), 5.04 (s, 1H), 5.24 (s, 1H), 5.93 (s, 2H), 6.80 (m, 3H). ^{13}C NMR: δ 13.6, 22.1, 29.6, 31.3, 76.7, 100.6, 106.8, 107.6, 108.9, 120.0, 136.0, 146.7, 147.4, 150.8. IR: 3390, 2957, 2930, 2873, 1650, 1503, 1487, 1442, 1247, 1094, 1041, 951, 933, 809. MS: *m/z* (relative intensity) 234 (100, [M$^+$]), 177 (14), 151 (67), 123 (11), 93 (15).

Representative Procedure for the $CrCl_2$-Catalyzed Reaction of Alkynyl Halides with Aldehydes. 5-Dodecyn-7-ol (17). To a stirred suspension of $CrCl_2$ (26 mg, 0.21 mmol), $NiCl_2$ (9 mg, 0.7 mmol), and Mn powder (120 mg, 2.1 mmol) in THF (7 mL) were added successively hexanal (125 mg, 1.25 mmol) and 1-iodo-1-hexyne (520 mg, 2.5 mmol). After the mixture was stirred for 6 h at ambient temperature, water (10 mL) was added and the stirring continued for 3 h until the silyl ether was quantitatively cleaved. The mixture was extracted with ethyl acetate in three portions (30 mL each), the combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated, and the residue was purified by flash chromatography with hexane/ethyl acetate (10/1) as eluent, affording the title compound as pale yellow syrup (180 mg, 79%). ^{1}H NMR: δ 4.38 (tt, 1H, J = 2, 6.4), 2.25 (dt, 2H, J = 2, 6.8), 1.78 (s, 1H, OH), 1.34−1.75 (m, 12H), 0.95 (t, 3H), 0.94 (t, 3H). ^{13}C NMR: δ 85.1, 81.0, 62.4, 37.8, 31.1, 30.4, 24.5, 22.2, 21.5, 18.0, 13.6, 13.2. IR: 3346, 2957, 2933, 2861, 2232, 1466, 1432, 1379, 1329, 1261, 1148, 1109, 1026, 914. MS: *m/z* (relative intensity) 182 (0.2, [M$^+$]), 153 (2), 139 (4), 125 (18), 111 (100), 55 (17).

1-Phenyl-2-heptyn-1-ol (18). Obtained according to the procedure outlined above as a pale yellow syrup. ^{1}H NMR: δ 7.24−7.55 (m, 5H), 5.42 (t, 1H, J = 1), 2.26 (dt, 3H, J = 1, 6.8), 1.32−1.60 (m, 4H), 0.91 (t, 3H, J = 7). ^{13}C NMR: δ 141.0, 128.2, 127.8, 126.3, 87.3, 79.6, 64.5, 30.3, 21.6, 18.2, 13.2. IR: 3374, 3064, 3031, 2958, 2933, 2872, 2280, 2227, 1603, 1493, 1454, 1430, 1379, 1328, 1192, 1135, 1002, 758, 726, 698, 635. MS: *m/z* (relative intensity) 188 (100, [M$^+$]), 187 (24), 145 (53), 131 (21), 117 (24), 115 (23), 105 (14), 91 (20), 77 (23).

Representative Procedure for the $CrCl_2$-Catalyzed Reaction of Allyl Halides with Aldehydes. 2-Methyl-1-phenyl-3-buten-1-ol (24). To a stirred suspension of $CrCl_2$ (22 mg, 0.18 mmol) and Mn (230 mg, 4.2 mmol) in THF (10 mL) was added successively benzaldehyde (265 mg, 2.5 mmol), (*E*)-crotyl bromide (675 mg, 5.0 mmol), and TMSCl (0.75 mL, 6.0 mmol). The mixture was stirred for 6 h at ambient temperature, the reaction was quenched by adding water (10 mL), and the mixture was stirred for another 3 h to ensure complete desilylation of the crude silyl ether. A standard extractive workup with ethyl acetate followed by flash chromatography with hexane/ethyl acetate (30/1) afforded the title homoallyl alcohol as a colorless syrup (320 mg, 79%). The isomeric ratio of the crude product is *threo*:*erythro* = 94:6 (GC).[1d,35] *Threo*-isomer. ^{1}H NMR: δ 7.22−7.36 (m, 5H), 5.81 (ddd, 1H, J = 7.9, 9, 17), 5.22 (dd, 1H, J = 1, 17), 5.16 (dd, 1H, J = 2, 9), 4.35 (d, 1H, J = 7.9), 2.53 (m, 1H), 2.19 (s, 1H, OH), 0.85 (d, 3H, J = 6.7). ^{13}C NMR: δ 142.5, 140.7, 128.2, 127.6, 126.5, 116.7, 77.9, 46.2, 16.5. IR: 3425, 3065, 3030, 2975, 2931, 2872, 1639, 1604, 1494, 1454, 1417, 1372, 1197, 1021, 915, 761, 701. MS: *m/z* (relative intensity) 162 (0.1, [M$^+$]), 107 (100), 79 (58), 77 (25). Diagnostic data of the *erythro*-isomer. ^{1}H NMR: δ 4.57 (d, J = 5.4), 0.99 (d, J = 6.9). ^{13}C NMR: δ 44.7, 14.0.

The following products have been obtained analogously.

1-Undecen-4-ol (2a). Colorless syrup. ^{1}H NMR: δ 0.81 (m, 3H), 1.21 (m, 8H), 1.38 (m, 2H), 2.00−2.34 (m, 3H), 3.63 (m, 1H), 5.05 (m, 1H), 5.13 (m, 1H), 5.69−5.90 (m, 1H). ^{13}C NMR: δ 13.7, 22.3, 25.3, 28.9, 29.2, 31.5, 36.4, 41.5, 70.5, 117.6, 134.5. IR: 3357, 3077, 2957, 2928, 2856, 1641, 1466, 1438, 1378, 1342, 1126, 1074, 1044, 994, 912. MS: *m/z* (relative intensity) 170 (0.3, [M$^+$]), 129 (24), 111 (22), 69 (100), 55 (36).

2-Methylene-4-(2-phenyl-1-ethyl)butyrolactone (20). Colorless syrup. ^{1}H NMR: δ 1.82−2.13 (m, 2H), 2.58 and 3.04 (dtAB system, 2H, J = 2.5, 7.8, 17), 2.76 (m, 2H), 4.52 (m, 1H), 5.62 (t, J = 2.5, 1H), 6.23 (t, J = 2.5, 1H), 7.15−7.34 (m, 5H). ^{13}C NMR: δ 31.0, 33.2, 37.7, 76.2, 121.8, 125.9, 128.1, 128.2, 134.3, 140.3, 169.9. IR: 3027, 2932, 2861, 1762, 1665, 1603, 1497, 1454, 1398, 1342, 1278, 1265, 1164, 1128, 1023, 937, 814, 752, 701, 627. MS: *m/z* (relative intensity) 202 (18, [M$^+$]), 117 (100), 91 (71).

3-Methyl-1-nonen-4-ol (25). *Threo*:*erythro* = 92:8 (GC).[36] Colorless syrup. *Threo*-isomer. ^{1}H NMR: δ 5.68−5.85 (m, 1H), 5.04−5.15 (m, 2H), 3.36−3.44 (m, 1H), 2.22 (virt-hex, 1H), 1.68 (s, 1H, OH), 1.31−1.49 (m, 10H), 1.03 (d, 3H, J = 6.9), 0.90 (vt, 3H, J = 6.4). ^{13}C NMR: δ 140.4, 116.0, 74.7, 44.0, 34.2, 31.9, 25.4, 22.6, 16.2, 14.0, 13.7. IR: 3382, 3076, 2959, 2931, 2860, 1639, 1460, 1417, 1378, 1260, 1121, 1096, 1000, 912. MS: *m/z* (relative intensity) 156 (6, [M$^+$], 101 (43), 99 (24), 83 (100), 56 (88), 55 (74), 43 (18), 41 (22). Diagnostic data for the *erythro*-isomer. ^{1}H NMR: δ 1.02 (d, J = 6.9). ^{13}C NMR: δ 140.8, 115.0.

(1*S,2*S**)-2,6-Dimethyl-2-ethenyl-1-phenyl-5-hepten-1-ol (29).** Colorless syrup.[8c] Isomeric ratio *S**,*S**:*R**,*S** = 94:6 (GC). Major isomer. ^{1}H NMR: δ 7.30−7.40 (m, 5H), 5.92 (dd, 1H, J = 10.8, 17.5), 5.33 (dd, 1H, J = 1.5, 10.8), 5.15 (dd, 1H, J = 1.5, 17.5), 5.05−5.22 (m, 1H), 4.47 (s, 1H), 2.02 (br s, 1H, OH), 1.92 (q, 2H), 1.71 (d, 3H, J = 1), 1.61 (s, 3H), 1.22−1.56 (m, 2H), 0.98 (s, 3H). ^{13}C NMR: δ 143.6, 140.1, 130.9, 127.7, 127.1, 127.0, 124.4, 115.5, 79.7, 45.6, 37.2, 25.3, 22.5, 17.3, 15.9. IR: 3448, 3083, 3030, 2969, 2925, 2857, 1637, 1604, 1493, 1453, 1413, 1375, 1189, 1083, 1048, 1012, 915, 730, 703. MS: *m/z* (relative intensity) 244 (0.6, [M$^+$]), 138 (31), 123 (36), 107 (100), 95 (80), 82 (11), 79 (55), 77 (28), 69 (97), 41 (40).

4-Methyl-1-decen-4-ol (22). ^{1}H NMR: δ 5.85 (X part of ABX, 1H), 5.05−5.16 (AB part of ABX, 2H), 2.22 (d, 2H, J = 7.4), 1.60 (br s, 1H, OH), 1.28−1.50 (m, 10H), 1.16 (s, 3H), 0.89 (vt, 3H). ^{13}C NMR: δ 133.8, 118.1, 71.8, 45.9, 41.5, 31.5, 29.5, 26.3, 23.4, 22.2, 13.7. IR: 3395, 3076, 2959, 2932, 2859, 1641, 1465, 1376, 1141, 1103, 1081, 1046, 998, 913. MS: *m/z* (relative intensity) 152 (5), 129 (49), 95 (13), 85 (21), 69 (61), 55 (27), 43 (100).

Representative Procedure for $CrCl_3$-Catalyzed Reactions. Methyl 7-Hydroxy-8-methyl-9-decenoate (27). To a stirred suspension of $CrCl_3$ (27 mg, 0.17 mmol) and Mn (230 mg, 4.2 mmol) in THF (10 mL) were added successively methyl 7-oxoheptanoate (390 mg, 2.5 mmol), (*E*)-crotyl bromide (675 mg, 5.0 mmol), and TMSCl (0.75 mL, 6.0 mmol) at ambient temperature. Water was added after a reaction time of 6 h, and the stirring was continued for another 3 h to ensure

(35) The stereochemical assignment was made according to the data given in ref. 1d and in the following references: (a) Fujita, K.; Schlosser, M. *Helv. Chim. Acta* **1982**, *65*, 1258−1263. (b) Gambaro, Marton, D.; Peruzzo, V.; Tagliavini, G. *J. Organomet. Chem*. **1982**, *226*, 149−155.

(36) Stereochemical assignment by comparison with the data reported in the following: Furlani, D.; Marton, D. *J. Chromatogr*. **1986**, *369*, 313−320.

complete desilyation of the crude product mixture. A standard extractive workup (EtOAc) followed by a flash chromatography with hexane/ethyl acetate (4/1) afforded the title compound as colorless syrup (450 mg, 83%). *Threo*:*erythro* = 92:8 (GC). *Threo*-isomer. ^{1}H NMR: δ 5.66−5.84 (m, 1H), 5.04−5.13 (m, 2H), 3.67 (s, 3H), 3.38 (m, 1H), 2.31 (t, 2H, J = 6.5), 2.17 (m, 1H), 1.78 (s, 1H, OH), 1.20−1.70 (m, 8H), 1.02 (d, 3H, J = 6.9). ^{13}C NMR: δ 173.9, 139.9, 115.8, 74.2, 51.1, 43.8, 33.6, 28.8, 28.7, 25.0, 24.5, 15.9. IR: 3462, 3076, 2936, 2861, 1740, 1639, 1457, 1437, 1419, 1370, 1256, 1203, 1174, 1002, 913. MS: *m/z* (relative intensity) 159 (18), 127 (100), 81 (76), 55 (29). Diagnostic data of the *erythro*-isomer. ^{13}C NMR: δ 140.6, 114.9, 43.1, 13.7.

Representative Procedure for Cp_2Cr-Catalyzed Reactions. To a suspension of Cp_2Cr (9 mg, 0.05 mmol) and Mn powder (230 mg, 4.2 mmol) in THF (7 mL) were added successively allyl bromide (0.42 mL, 5.0 mmol), octanal (0.39 mL, 2.5 mmol), and TMSCl (0.75 mL, 6.0 mmol). The dark blue suspension slowly turned gray due to the precipitation of white manganese salts. After the mixture was stirred overnight at ambient temperature, water (10 mL) was added and the stirring continued for another 2 h to ensure quantitative desilylation of the crude product. An extractive workup as described above followed by flash chromatography (hexane/ethyl acetate = 30/1) afforded alcohol **2a** as colorless syrup (312 mg, 73%). The spectroscopic data are in full agreement with those compiled above.

Representative Procedure for $CpCrCl_2$·THF-Catalyzed Reactions. To a suspension of Mn powder (460 mg, 8.4 mmol) and $CpCrCl_2$·THF (13 mg, 0.05 mmol) in THF (10 mL) were added octanal (0.78 mL, 5.0 mmol), (*E*)-crotyl bromide (1.02 mL, 10.0 mmol), and TMSCl (1.5 mL, 12 mmol). The suspension was stirred for 6 h at ambient temperature, the reaction was quenched by adding water (10 mL), and the stirring was continued (2 h) until TLC showed complete desilylation of the crude product mixture. A standard extractive workup as described followed by flash chromatography (hexane/ethyl acetate = 30/1) gave compound **26** as a colorless syrup (853 mg, 92%). The diastereomeric ratio of the crude product was determined by GC as *anti*:*syn* = 78:22 in analogy to ref 36. *Threo*-isomer. ^{1}H NMR: δ 5.68−5.89 (m, 1H), 5.03−5.14 (m, 2H), 3.39−3.50 (m, 1H), 2.21−2.35 (m, 1H), 1.15−1.63 (m, 13H), 1.07 (d, 3H, J = 6.9), 0.91 (t, 3H). ^{13}C NMR: δ 140.0, 115.8, 74.4, 43.7, 33.9, 31.5, 29.3, 28.9, 25.4, 22.3, 15.9, 13.7. IR: 3379, 3077, 2959, 2928, 2856, 1639, 1459, 1418, 1378, 998, 912. MS: *m/z* (relative intensity) 184 (0.5, [M^+]), 129 (12), 111 (18), 69 (99), 56 (100). Diagnostic data of the *erythro*-isomer. ^{13}C NMR: δ 140.8, 114.7, 43.1.

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