Journal of Organometallic Chemistry 695 (2010) 2180–2190

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Gold-catalyzed stereoselective reaction of tricarbonylchromium complexes of *ortho*-alkynyl benzaldehydes and benzaldimines with nucleophiles

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ARTICLE INFO

Article history:
Received 11 May 2010
Received in revised form
31 May 2010
Accepted 3 June 2010
Available online 15 June 2010

Keywords:
Arene chromium complex
Dihydroisoquinoline
Gold catalysis
Isochroman
Planar chirality

ABSTRACT

Gold(I)-catalyzed reaction of *ortho*-alkynyl benzaldehyde tricarbonylchromium complexes with nucleophiles gave stereoselectively 1-*anti*- and *syn*-functionalized 1*H*-isochromene chromium complexes depending on the nature of nucleophile. By reaction with alcohols, 1-*anti*-alkoxy 1*H*-isochromene tricarbonylchromium complexes were obtained *via* gold benzopyrylium-type intermediates. On the other hand, carbon nucleophiles gave 1-*syn*-functionalized 1*H*-isochromene chromium complexes *via* stereoselective addition of nucleophiles to the activated carbonyl group and following cyclization. Methoxy group of 1-*anti*-methoxy-1*H*-isochromene chromium complex was substituted with carbon nucleophiles in the presence of Lewis acid to afford 1-*anti*-functionalized 1*H*-isochromene chromium complexes. These methods can be applied to the synthesis of enantiomerically pure *trans*- and *cis*-1,3-dimethylisochromans starting from a single planar chiral chromium complex. Similarly, *ortho*-alkynyl benzaldimine tricarbonylchromium complexes gave stereoselectively 1-*syn*- and *anti*-functionalized dihydroisoquinoline chromium complexes by gold(I)-catalyzed reaction with nucleophile.

1. Introduction

Oxygen and nitrogen heterocycles are common structural components of a wide range of naturally occurring and biologically active molecules [1]. Development of new and efficient methods for the synthesis of heterocyclic compounds is of central importance in organic synthesis. An attractive route to the synthesis of functionalized heterocycles is *via* X–H bond of nitrogen or oxygen nucleophile across the carbon–carbon multibond. An activation of the triple bond is normally required for the achievement of this process. Thus, halogens [2], ArSeBr, ArSCl, Ipy_2BF_4 [3] or transition metals [4] such as palladium, silver, gold or indium catalysts are employed for the activation of alkyne bond. Transition metal-catalyzed electrophilic activation of alkynes has attracted much attention as a useful method, and the generated metal-containing benzopyrylium-type intermediates is considered a common process, which upon further treatment with various partners, such as nucleophiles, alkynes, alkenes and carbonyl compounds, result in diverse products [5]. In particular, gold has emerged as a powerful homogeneous catalyst for the electrophilic activation of alkynes, and has been demonstrated in useful organic transforming reactions [6]. The metal-catalyzed reaction of *o*-alkynyl benzaldehydes with nucleophiles giving 1-functionalized-1*H*-isochromenes is still attractive reaction. However, the cyclized 1-functionalized heterocycles by this methodology are usually achiral compound, although a chiral center is created. Directed toward the synthesis of optically active heterocycles, we employed planar chiral arene chromium complex in this study. In the case of chromium-complexed *o*-alkynyl benzaldehydes, the structure of metal-coordinated interemediates is a significant factor for relative stereochemistry of the cyclized 1-functionalized 1*H*-isochromene tricarbonylchromium complexes. Three activation modes by the coordination with metal are devised (Fig. 1). In the transition state **A**, metal activates the carbonyl group in which carbonyl oxygen is an *anti*-conformation with *ortho* alkyne substituent due to a steric interaction. On the other hand, the alkyne in the intermediate **B** is activated by metal e.g. Au(I) and Pd(II)/Cu(II) systems giving metal-contained benzopyrylinium ion intermediate [7].

The transition state **C** has dual carbophilic and oxophilic activations [8] with metal such as $In(OTf)_3$ catalyst at the same time. Since nucleophiles attack the metal-coordinated intermediates from an opposite side with tricarbonylchromium fragment, the relative stereochemistry at the benzylic position of cyclized 1-functionalized 1*H*-isochromene chromium complexes derived from the transition state **A** is distinct from the other intermediates **B** and **C**. Thus, the substituent at the benzylic position of cyclized isochromene chromium complexes derived from the transition state **A** would be a *syn*-configuration with tricarbonylchromium fragment, while the

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doi:10.1016/j.jorganchem.2010.06.005

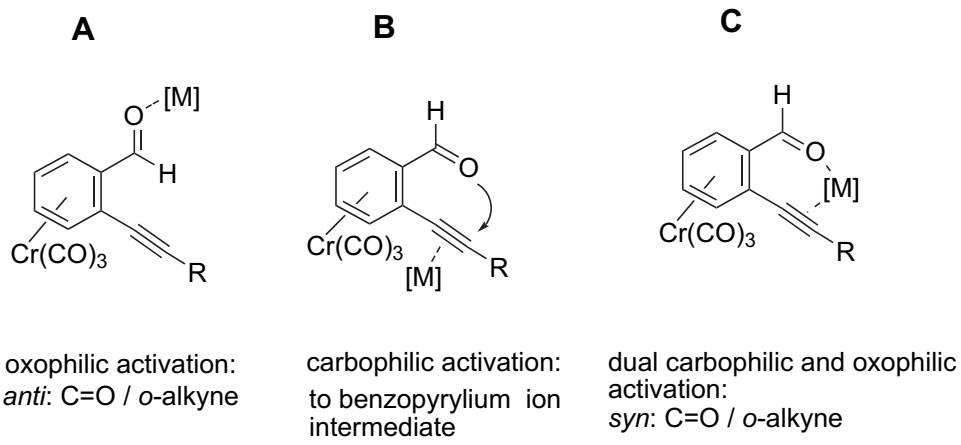


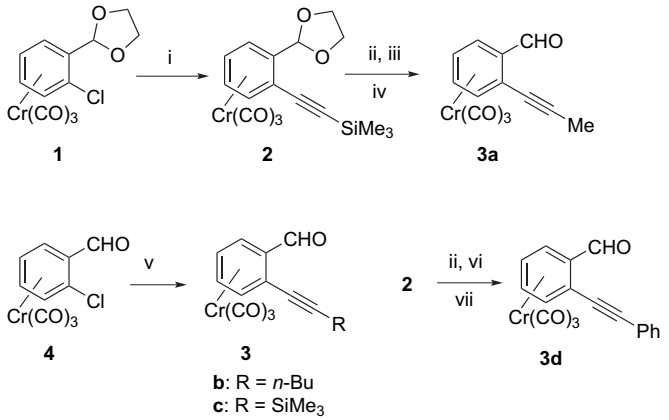
Fig. 1. Activated form of *o*-alkynylbenzaldehyde chromium complex with metal.

corresponding substituent arised from the coordination states **B** or **C** is an *anti*-configuration. Herein, we describe the full details of the scope and limitations of gold(I)-catalyzed electrophilic cyclization of the planar chiral chromium complexes of *ortho*-alkynyl benzaldehydes and benzaldimines with nucleophiles [9].

2. Results and discussion

Gold(I)-catalyzed reaction of o-alkynyl benzaldehyde tricarbonylchromium complexes. ortho-alkynyl benzaldehyde tricarbonylchromium complexes as starting materials in this study were prepared from benzaldehyde ethyleneacetal chromium complex (Scheme 1). Sonogashira coupling of *o*-chlorobenzaldehyde ethyleneacetal chromium complex **1** with trimethylsilylacetylene gave a coupling product **2** in good yield. Deprotection of **2** with aqueous NaOH at −20 °C followed by methylation and subsequently hydrolysis produced [2-(prop-1-ynyl)benzaldehyde]tricarbonylchromium (**3a**) in good yield. Other *ortho*-alkynyl benzaldehyde chromium complexes **3b** and **3c** were prepared by Sonogashira coupling of *ortho*-chlorobenzaldehyde chromium complex **4** with substituted-alkynes [10]. 2-Phenylethynyl benzaldehyde chromium complex **3d** was obtained by detrimethylsilylation, acidic hydrolysis of acetal and finally Sonogashira coupling with iodobenzene from chromium complex **2**.

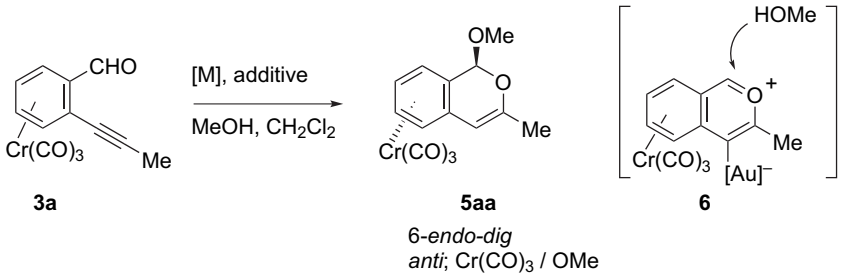
An effect of the metal catalyst for activation of the alkyne bond of 2-(prop-1-ynyl)benzaldehyde chromium complex (**3a**) was initially examined. As shown in Table 1, metal such as Ag(I), Pd(II) and $In(OTf)_3$ gave no cyclization product by reaction of the complex **3a** with MeOH, while the corresponding chromium-free *o*-alkynyl benzaldehyde afforded cyclized 1-methoxy-1*H*-isochromene by reaction with these catalysts [4–6]. With both Au(III) and Au(I) catalysts, cyclized isochromene chromium complex **5aa** was also not observed (entries 4 and 5). No cyclization product might be contributed a decreased electron-density of the alkyne bond due to a strong electron-withdrawing ability of the tricarbonylchromium fragment. However, an addition of silver salt for de-chlorination of PPh_3AuCl catalyst gave 6-*endo-dig* cyclization product **5aa** as a single diatereomer in moderate yields (entries 6–8). The best result was obtained by using of isolated gold bis(trifluoromethanesulfonyl)imidate [11], PPh_3AuNTf_2, in methylene chloride at room temperature (entry 9). This catalyst enhances the Lewis acidity for the coordination to alkyne bonds. It is noteworthy



Reagents and conditions: i) trimethylsilylacetylene, 5 mol% $Pd(PPh_3)_2Cl_2$, 5 mol% CuI, Et_3N, THF, reflux, 30 min (87%); ii) 2N NaOH, MeOH, –20 °C (87%); iii) MeLi, THF, –50 °C, then MeI (85%); iv) 6N HCl, THF, 0° to rt (95%); v) 1-alkyne, 5 mol% $Pd(PPh_3)_2Cl_2$, 5 mol% CuI, Et_3N, THF (79% for R = *n*-Bu, 82% for R = $SiMe_3$); vi) 6N HCl, THF (88%); vii) Iodobenzene, 6 mol% $Pd(PPh_3)_4$, 7mol% CuI, THF, NEt_3, rt, then 45 °C (99%)

Scheme 1. Synthesis of *o*-alkynylbenzaldehyde tricarbonylchromium complexes.

Table 1
Metal-catalyzed reaction of *o*-propynylbenzaldehyde chromium complex **3a** with MeOH.



3a **5aa** **6**

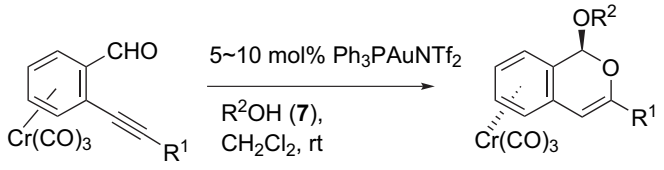
6-*endo-dig*
anti; $Cr(CO)_3$ / OMe

Entry	[M]	Additive	Conditions	Yield (%)
1	$Pd(OAc)_2$	Benzoquinone	Dioxane, 80 °C	–
2	$In(OTf)_3$	–	DMF, 50 °C	–
3	AgOTf	–	CH_2Cl_2, reflux	–
4	$AuCl_3$	–	$(CH_2Cl)_2$, 80 °C	–
5	PPh_3AuCl	–	CH_2Cl_2, 40 °C	–
6	PPh_3AuCl	AgOTf	CH_2Cl_2, rt	44
7	PPh_3AuCl	$AgSbF_6$	CH_2Cl_2, rt	59
8	PPh_3AuCl	$AgBF_4$	CH_2Cl_2, rt	Trace
9	PPh_3AuNTf_2	–	CH_2Cl_2, rt	80

that the reaction proceeds under mild condition (room temperature, within 30 min), while the corresponding chromium-free *o*-alkynyl benzaldehydes were required high reaction temperature and long reaction time. The *anti*-stereochemistry of the methoxy group of **5aa** was determined by X-ray crystallography [12]. The cyclized isochromene chromium complex **5aa** was derived from an *anti*-atack of methanol to the generated chromium-complexed benzopyrinium intermediate **6** derived from the transition state **B**.

Having established the optimal reaction conditions, we explored the scope of the methodology by subjecting a range of *o*-alkynyl benzaldehyde chromium complexes with various alcohols and the results are summarized in Table 2. The reaction took place stereo and regioselectively with primary and secondary alcohols in good yields. TMS-substituted alkyne chromium complex **3c** gave also 6-*endo-dig* cyclization product (entry 6), while treatment of **3c** with 2 M aqueous NaOH in MeOH at room temperature produced exclusively 5-*exo-dig* cyclization product with loss of TMS group (*vide infra*). The benzaldehyde chromium complex **3e** without substituent at the alkyne terminus gave a complexed mixture by gold-catalyzed reaction under same conditions (entry 8).

Table 2
Gold(I)-catalyzed reactionof *o*-alkynyl benzaldehyde chromium complexes with alcohols.



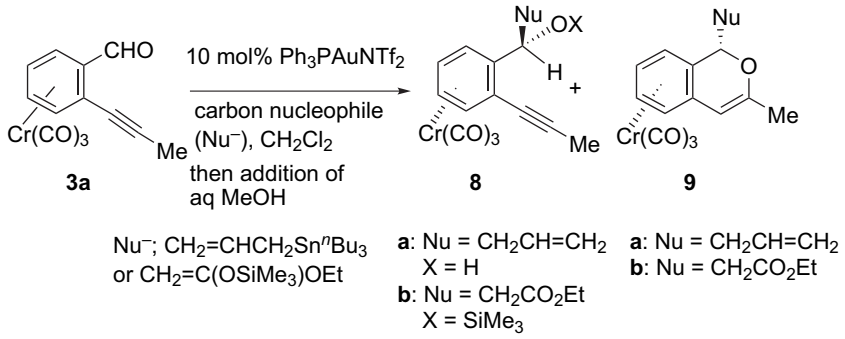
3 **5**

Entry	**3**	R^1	R^2OH (**7**)	**5**	Yield (%)
1	**3a**	Me	MeOH (**7a**)	**5aa**	80
2	**3a**	Me	^{i}PrOH (**7b**)	**5ab**	60
3	**3a**	Me	CH_2=$CHCH_2OH$ (**7c**)	**5ac**	83
4	**3a**	Me	CH=CCH_2OH (**7d**)	**5ad**	62
5	**3b**	*n*Bu	MeOH (**7a**)	**5ba**	71
6	**3c**	$SiMe_3$	MeOH (**7a**)	**5ca**	66
7	**3d**	Ph	MeOH (**7a**)	**5da**	73
8[a]	**3e**	H	MeOH (**7a**)	**5ea**	–

[a] Complexed mixture.

We next turned our attention to the gold(I)-catalyzed reaction of *o*-alkynyl benzaldehyde tricarbonylchromium complexes with carbon pronucleophiles. Treatment of **3a** with allyl tri-*n*-butylstannane in the presence of 10 mol% gold(I) catalyst at room temperature for 4.5 h gave interestingly 1-*syn*-allyl-1*H*-isochromene chromium complex **9a** in 17% yield, along with the formation of a single diastereomeric allylated benzylalcohol chromium complex **8a** in 40% yield (Scheme 2). The corresponding *anti*-allyl-1*H*-isochromene chromium complex was not detected. The *syn* stereochemistry of allyl group of the cyclization product **9a** was confirmed by X-ray crystallography [12]. Similarly, ketene trimethylsilyl ethyl acetal afforded a mixture of *syn*-functionalized isochromene chromium complex **9b** and benzylalcohol trimethylsilyl ether **8b** in 19% and 38% yields, respectively, by treatment with the Au(I) catalyst at −20 °C for 10 min and following reflux for overnight after addition of 10 equivalent MeOH and H_2O. The *syn*-functionalized 1*H*-isochromene chromium complexes **9a** and **9b** would be formed *via* diastereoselective nucleophilc addition to an *anti*-oriented carbonyl group in the metal-coordinated intermediate **A** and subsequent intramolecular cyclization of hydroxy group with metal-activated alkyne group. Different *anti*- vs *syn*-stereoselectivity of the cyclization products depending on the employing nucleophiles would be fundamentally contributed to a different ability of nucleophilic addition to the carbonyl group. With carbon nucleophile, the addition to carbonyl group takes place exclusively giving a single diastereomeric addition product. Consequently, the cyclization products are *syn*-isomers. Thus, gold bis(trifluoromethanesulfonyl)imidate catalysis in the reaction of chromium-complexed *o*-alkynyl benzaldehyde with carbon nucleophile serves as a multicatalysis [13] for the activation of carbonyl and subsequently alkyne groups with catalytic transformation stepwise. The low yield of the cyclized isochromene chromium complexes **9** would be contributed to a slow cleavage of the generated benzyl alkoxide intermediate, and a decrease of the activity of the gold catalyst by addition of aqueous methanol.

The low yield of 1-*syn*-functionalized isochromene chromium complexes **9** by one pot synthesis was improved by stepwise reaction *via* benzylalcohol derivatives as follows. The chromium



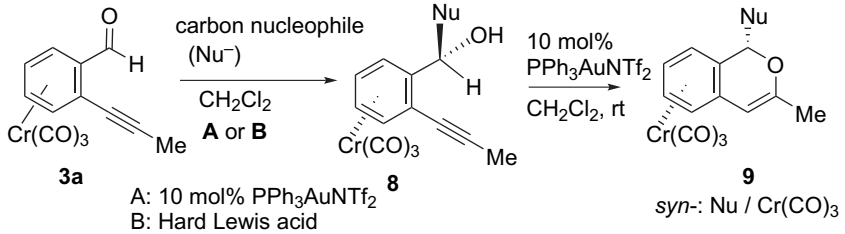
Scheme 2. Gold(I)-catalyzed reaction of *o*-alkynylbenzaldehyde chromium complex with carbon nucleophile.

complex **3a** was reacted with allyl tri-*n*-butylstannane in the presence of 10 mol% $(Ph_3P)AuNTf_2$ in CH_2Cl_2 at −20 °C to give a diastereomerically single allylated secondary benzylalcohol chromium complex **8a** in 73% yield (Table 3, entry 1). Similarly, ketene enolsilyl acetal and diethylalumium acetylide produced the corresponding benzyl alcohol chromium complexes **8b**, **8c** (entries 2, 3). The other hard Lewis acid such as $BF_3\cdot OEt_2$ or $TiCl_4$ can be also employed. Methyl lithium reacted without Lewis acid to afford a diastereomerically single phenylethyl alcohol chromium complex in good yield (entry 4). The obtained *o*-alkynyl benzyl alcohol chromium complexes **8** were treated with 10 mol% gold(I) catalyst at room temperature to give 1-*syn*-functionalized 1*H*-isochromene chromium complexes **9** without formation of the corresponding 5-*exo*-*dig* cyclization products [14,15b].

We next studied substitution of the alkoxy group of 1-*anti*-alkoxy 1*H*-isochromene chromium complex with carbon nucleophiles for further manipulation. Chromium-complexed benzylic position could be stabilized as benzylic cations and the property has been widely employed for useful stereoselective carbon–carbon bond forming reactions [15]. Treatment of 1-*anti*-methoxy-1*H*-isochromene chromium complex (**5aa**) with carbon nucleophiles in the presence of Lewis acid gave 1-*anti*-functionalized 1*H*-isochromene chromium complexes **10** (Table 4). Alkyl, allyl, ester, nitrile and alkyne groups can be introduced stereoselectively. In this manner, both 1-*anti*- and 1-*syn*-functionalized 1*H*-isochromene tricarbonylchromium complexes can be stereoselectively prepared from a single *o*-substituted benzaldehyde chromium complex. Thus, the gold(I)-catalyzed reaction of *o*-alkynyl benzaldehyde chromium complexes with alcohols gave 1-*anti*-alkoxy 1*H*-isochromene chromium complexes which were subsequently treated with carbon nucleophiles in the presence of Lewis acid to afford stereoselectively 1-*anti*-functionalized 1*H*-isochromene tricarbonylchromium complexes. On the other hand, the gold(I)-catalyzed reaction of *o*-alkynyl benzaldehyde chromium complexes with carbon nucleophiles produced 1-*syn*-functionalized 1*H*-isochromene tricarbonylchromium complexes *via* secondary benzylalcohol chromium complexes. Both reaction sequences are useful for stereoselective synthesis of functionalized isochromans.

These reaction sequences could be applied to the synthesis of enantiomerically pure *trans*- and *cis*-1,3- dimethylisochromans as shown in Scheme 3. Diastereoselective *ortho* lithiation [16] of (+)-(benzylidene)methyl-α-D-glucopyranoside chromium complex **11** followed by bromination with 1,2-dibromo-1,1,2,2-tetrafluoroethane gave (+)-*o*-brominated chromium complex **12**. (+)-*ortho*-brominated chromium complex **12** was converted to (−)-*o*-(prop-1-ynyl)benzaldehyde tricarbonylchromium complex (**13**) with 99% ee by several steps. The chromium complex **13** was reacted with MeOH in the presence PPh_3AuNTf_2 followed by treatment with Me_3Al to give (−)-1-*anti*-methyl-3-methyl-1*H*-isochromene chromium complex (**14**) in good yield. Reduction of double bond of the complex **14** with Et_3SiH/CF_3CO_2H followed by air

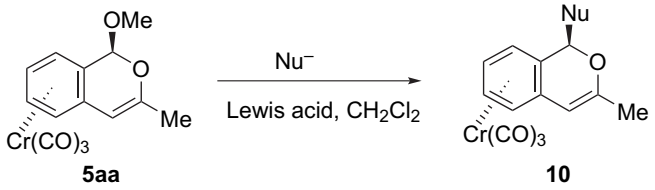
Table 3
Two steps synthesis of 1-*syn*-functionalized isochromene tricarbonylchromium complexes.



Entry	Nu^-	Yield **8** (%)		**9**	Yield **9** (%)
		A	**B** (Lewis acid)		
1	$CH_2{=}CHCH_2Sn(n\text{-}Bu)_3$	73	60 ($BF_3.OEt_2$)	**9a** (Nu = $CH_2CH{=}CH_2$)	68
2[a]	$CH_2{=}C(OSiMe_3)OEt$	56	58 (TiCl4)	**9b** (Nu = CH_2CO_2Et)	69
3	$Et_2AlC{=}CBu^n$	97	–	**9c** (Nu = $C{=}CBu^n$)	31
4	MeLi	91[b]	–	**9d** (Nu = Me)	80

[a] TBAF was added to the reaction mixture for deprotection of O–$SiMe_3$ bond.
[b] The reaction took place in ether at −78 °C without Au(I) or Lewis acid.

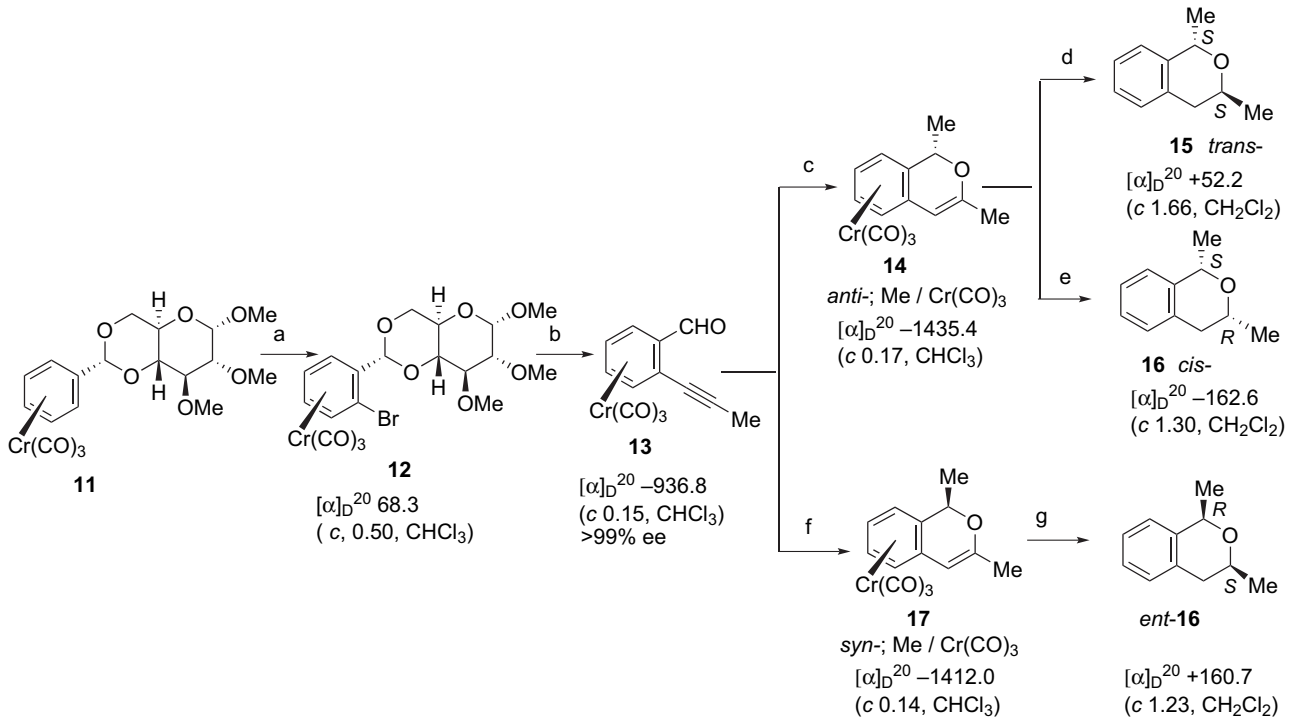
Table 4
Lewis acid mediated transformation of 1-*anti*-methoxy iochromene chromium complex **5aa**.



Entry	Nu–	Lewis acid	**10**	Nu	Yield (%)
1	Me_3Al	–	**10a**	Me	99
2	CH_2=$CHCH_2Sn(n\text{-}Bu)_3$	$BF3\cdot OEt_2$	**10b**	CH_2CH=CH_2	60
3	CH_2=$C(OSiMe_3)OEt$	$TiCl_4$	**10c**	CH_2CO_2Et	72
4	Me_3SiCN	$BF_3\cdot OEt_2$	**10d**	CN	56
5	Et_2AlC=CBu^n	$BF_3\cdot OEt_2$	**10e**	C=CBu^n	74

oxidation gave (+)-*trans*-1,3-dimethylisochroman (**15**) [17]. On the other hand, air oxidation of **14** and subsequent reduction with 10% Pd/C under 1 atmosphereic hydrogen afforded (−)-*cis*-1,3-dimethylisochroman (**16**) [17]. Furthermore, reaction of MeLi with (+)-benzaldehyde chromium complex **13** followed by gold(I)-catalyzed cyclization afforded (−)-1-*syn*-methyl-3-methyl-1*H*-isochromene chromium complex (**17**) in good yield. The chromium complex **17** was converted to (+)-*ent*-**16** by reduction of the double bond and subsequent photo-oxidation. In this way, enantiomerically pure *trans*- and both enantiomers of *cis*-1,3-dimethylisochromans were stereoselectively prepared from a single planar chiral arene chromium complex **13** (Scheme 3).

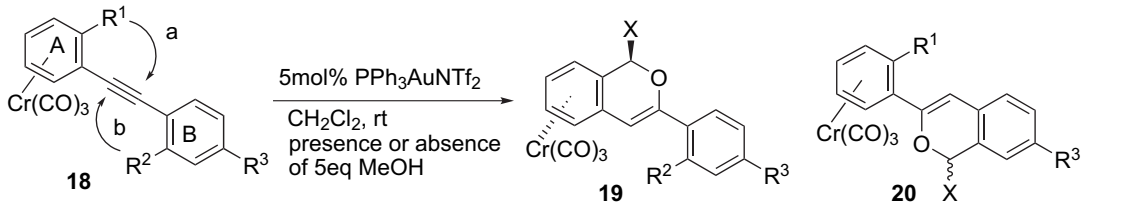
As a further extension of the stereoselective gold(I)-catalyzed reaction of *o*-alkynyl arene chromium complexes, we examined an effect of the tricarbonylchromium fragment on the regioselectivity of 6-*endo-dig* cyclization of mono tricarbonylchromium complexes of 1,2-bis(phenyl)acetylene substituted with nuclophilc functional groups at the *ortho* position of both arene rings. In the case of biaryl mono chromium complexes with an identical substituent at the *ortho* position of both arene rings, two directions of 6-*endo-dig* cyclization (path a or b) might be possible (Table 5, path a or b). If either of two direction modes takes place predominantly, further useful organic transformations could be developed. Gold(I)-catalyzed reaction of bis-benzaldehyde acetylene mono chromium complex **18a** in the presence of MeOH resulted in a recovery of the starting material without formation of the cyclized methoxy isochromene chromium complexes **19a** and **20a** (entry 1). However, regioisomeric bis-benzaldehyde chromium complex **18b** with *para* formyl group on the B-ring afforded an expected 1-*anti*-methoxy-1*H*-isochromene chromium complex **19b** under the same conditions (entry 2). On the other hand, bis-dihydroxymethyl substituted biaryl chromium complex **18c** gave a mixture of isochromene chromium complex **19c** as a minor product and a further cyclized spiro compound **21** as a major product by gold-catalyzed reaction without MeOH (entry 3). Structural isomeric cyclization product



Reagents and conditions
a) *n*-BuLi, ether, –78 ° to –40 °C; then BrF_2CCF_2Br, –40 ° to 0 °C (77%). b) (i) trimethylsilylacetylene, 5 mol% $Pd(PPh_3)_2Cl_2$, 5 mol% CuI, Et_3N, THF, 80 °C (97%); (ii) *n*-Bu_4NF, THF, 0 °C (97%); (iii) MeLi, ether, –50 °C, 1 h; then MeI, 0 °C (91%); (iv) 50% aq. H_2SO_4, acetone, rt (68%); c) (i) 5mol% PPh_3AuNTf_2, MeOH, CH_2Cl_2, rt (80%); (ii) Me_3Al, CH_2Cl_2, (72%); d) (i) Et_3SiH, CF_3CO_2H, CH_2Cl_2, –20 ~ 0 °C (75%); (ii) *h*ν/air, ether (quantitative); e) (i) *h*ν/air, ether (quantitative); (ii) 10%Pd/C, H_2,CH_2Cl_2, THF (quantitative); f) (i) MeLi, ether, –78°C (91%); (ii) 5 mol% PPh_3AuNTf_2, CH_2Cl_2, rt (80%); g) (i) Et_3SiH, CF_3CO_2H, CH_2Cl_2 (88%); (ii) *h*ν/air, ether.

Scheme 3. Stereoselective synthesis of enantiomerically pure 1,3-dimethylisochromans.

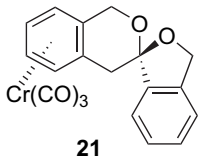
Table 5
Effect of $Cr(CO)_3$ to regioselectivity in gold(I)-catalyzed cyclization.



a: $R^1 = R^2 = CHO$, $R^3 = H$
b: $R^1 = R^3 = CHO$, $R^2 = H$
c: $R^1 = R^2 = CH_2OH$, $R^3 = H$
d: $R^1 = CHO$, $R^2 = CH_2OH$, $R^3 = H$
e: $R^1 = CH_2OH$, $R^2 = CHO$, $R^3 = H$

a: X = OMe, $R^2 = CHO$, $R^3 = H$
b: X = OMe, $R^2 = H$, $R^3 = CHO$
c: X = H, $R^2 = CH_2OH$, $R^3 = H$
d: X = OMe, $R^2 = CH_2OH$, $R^3 = H$
e: X = H, $R^2 = CHO$, $R^3 = H$

a: X = OMe, $R^1 = CHO$, $R^3 = H$
b: X = H, $R^1 = CHO$, $R^3 = H$
c: X = H, $R^1 = CH_2OH$, $R^3 = H$
d: X = OMe, $R^1 = CH_2OH$, $R^3 = H$



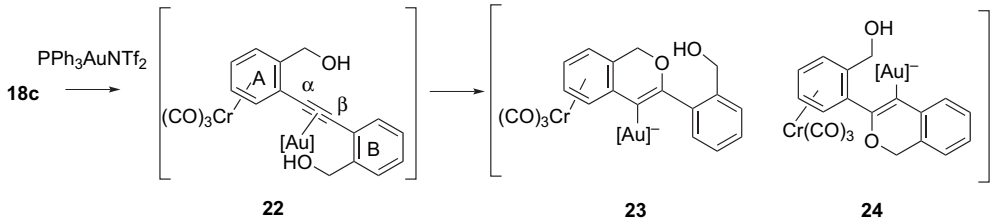
21

Entry	Complex **18**	MeOH	Products (yield %)
1[a]	**18a**	+	–
2	**18b**	+	**19b** (46)
3	**18c**	–	**19c** (13), **21** (59)
4	**18d**	+	**19d** (50)
5[a,b]	**18d**	–	–
6	**18e**	+	**20d**[c] (82)
7[b]	**18e**	–	–

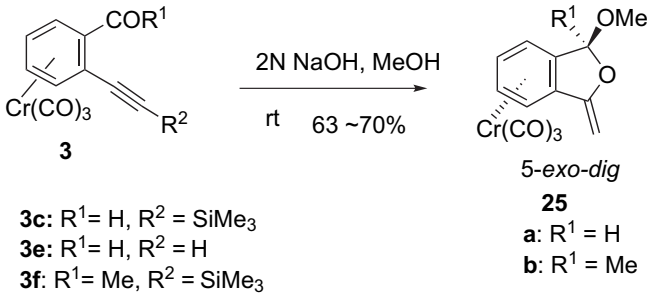
[a] Recovery of starting material.
[b] Complexed mixture.
[c] 1:1 diastereomeric mixture.

20c and further cyclized compound were not observed. This result indicates that the hydroxymethyl group of chromium-coordinated arene ring operated predominantly as the nucleophile. The regioselective cyclization would be contributed to a different electron-density at α- and β-carbons of the alkyne bond. Between two possible 6-*endo-dig* cyclized intermediates **23** and **24** generated from the gold-activated alkyne intermediate **22**, the chromium-complexed benzylic position (α-position) is more stabilized as an anion character due to the electron-withdrawing ability of the tricarbonylchromium fragment (Scheme 4) [18].

Furthermore, reactivity of the gold-catalyzed cyclization of bis-aryl alkyne mono chromium complexes with hydroxyymethyl and formyl groups under different reaction conditions was studied. *o*-Alkynyl benzaldehyde chromium complex **18d** with hydroxymethyl group on the B-ring produced expected 6-*endo-dig* cyclized 1-methoxy-1*H*-isochromene chromium complex **19d** by gold-catalyzed-reaction in the presence of methanol (entry 4), while the complex **18d** was treated in the absence of MeOH to result in a recovery of the starting material without formation of expected cyclization product **20b** (entry 5). On the other hand, *o*-alkynyl benzylalcohol chromium complex **18e** with formyl group on the B-ring gave a 1: 1 diastereomeric mixture of the cyclization product **20d** in the presence of MeOH (entry 6), while the complex **18e** afforded no cyclization product in the absence of MeOH (entry 7). Thus, the cyclized isochromene derivatives between the hydroxy group and activated alkyne bond were not formed under the absence of MeOH. In contrast with above conditions, the reaction under the presence of methanol as nucleophile gave expected 1-methoxy-isochromene derivatives in good yields. With biaryl substituted-alkynes with both formyl and hydroxymethyl groups at the *ortho* positions, the formyl group would attacks predominantly to the activated alkyne to give gold-containing benzopyrylium-type intermediate which will react with methanol to afford the cyclized product. In the case of absence of methanol, the starting materials are recovered since the generated benzopyrinium intermediate could not react with nucleophile.



Scheme 4. Proposed reaction mechanism.



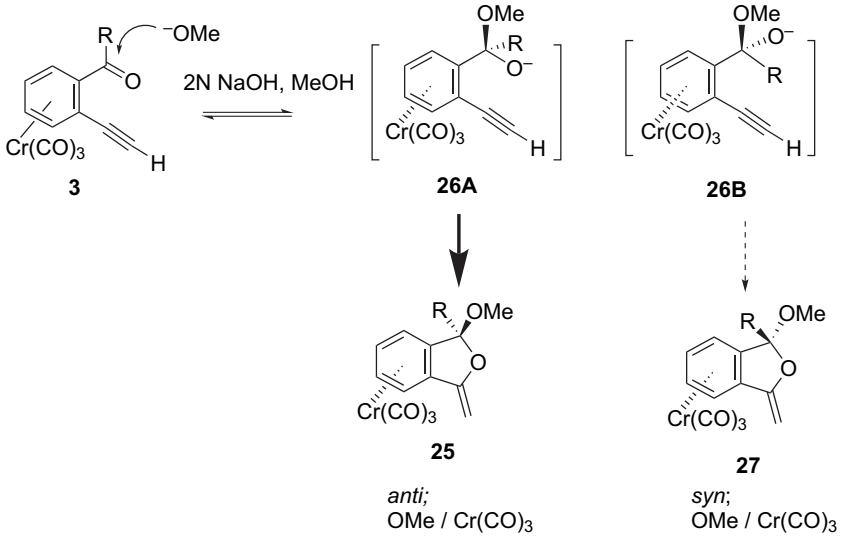
Scheme 5. Reaction of chromium complex with MeOH under basic conditions.

Base-catalyzed reaction of 2-alkynyl benzaldehyde chromium complexes. As mentioned above, gold(I)-catalyzed reaction of 2-alkynyl benzaldehyde chromium complexes with nucleophiles gave 6-*endo-dig* cyclization products. However, base-catalyzed reaction produced different cyclization mode product as follows. Thus, the treatment of [2-(trimethylsilylethynyl)benzaldehyde]tricarbonylchromium (**3c**) with aqueous NaOH in MeOH at room temperature gave regio- and stereoselectively 1-*anti*-methoxy-3-methylidene-1,3-dihydroisobenzofuran tricarbonylchromium (**25a**) in 64% yield (Scheme 5). The stereochemistry of OMe group of **25a** was determined as an *anti*-configuration by X-ray crystallography [12]. Similarly, terminal alkyne chromium complex **3e** afforded also 1-*anti*-methoxy-3-methylidene-1,3-dihydroisobenzofuran tricarbonylchromium (**25a**). Besides benzaldehyde chromium complexes, 2-alkynyl acetophenone chromium complex **3f** afforded stereoselectively 5-*exo-dig* mode cyclization product **25b** [12] as a single stereoisomer under the same conditions. In this way, the cyclization mode of *o*-alkynyl benzaldehyde chromium complexes is distinct between Au(I)-catalyzed reaction and base mediated cyclization.

A mechanism for the stereoselective formation of 5-*exo-dig* cyclization product **25** is proposed in Scheme 6. Under the basic conditions, alkoxide anion attacks the carbonyl group from an *exo*-side with the tricarbonylchromium fragment to generate diastereomeric hemiacetal intermediates **26A** and **26B** [19]. A diastereomeric hemiacetal intermediate **26A** will afford the *anti*-methoxy isobenzofuran complex **25** by subsequent intramolecular cyclization, while the other diastereomer **26B** produces the corresponding *syn*-isomer **27**. The formation of *anti*-isomer **25** *via* the intermediate **26A** from the chromium complex **3** takes place concertedly. On the other hand, the diastereomeric hemiacetal intermediate **26B** attains equilibrium to the parent carbonyl group, since the diastereomer **26B** is required a rotation between aryl and benzylic bond for the *syn*-isomer **27**.

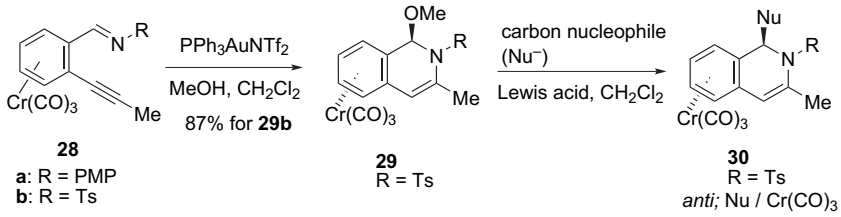
Gold(I)-catalyzed reaction of o-alkynyl benzaldimine tricarbonylchromium complexes. We furthermore studied the gold(I)-catalyzed reaction of *o*-alkynyl benzaldimine tricarbonylchromium complexes directed toward stereoselective synthesis of optically active 1,3-difunctionalized 1,2-dihydro- or tetrahydroisoquinoline derivatives (Table 6). *ortho*-Alkynyl benzaldimine chromium complexes **28** as starting materials were easily prepared from *o*-alkynyl benzaldehyde tricarbonylchromium **3a** and *p*-methoxyaniline or *p*-toluenesulfonamide [20]. Gold(I)-catalyzed reaction of *p*-methoxyphenyl substituted imine chromium complex **28a** with methanol or carbon nucleophile gave the corresponding cyclization or addition products in very low yield [21]. Reduction of **28a** with large excess of $NaBH_4$ afforded the corresponding benzylamine chromium complex, which was treated with PPh_3AuNTf_2 at room temperature to give 1,2-dihydroisoquinoline chromium complex in good yield. However, as the obtained 1,2-dihydroisoquinoline chromium complex has no functional group at C-1 position, gold-catalyzed reaction of an electron-withdrawing *p*-tosyl substituted imine chromium complex **28b** with nucleophiles was examined. Gold(I)-catalyzed reaction of **28b** with MeOH gave expectedly 1-*anti*-methoxy 1,2-dihydroisoquinoline chromium complex **29** in good yield. Subsequently, Lewis acid mediated-substitution of the methoxy group of **29** with carbon nucleophiles afforded 1-*anti*-functionalized 1,2-dihydroisoquinoline chromium complexes **30** as well as 1-methoxy-isochromene chromium complex in shown in Table 4.

Reaction of *o*-alkynyl benzaldimine chromium complex **28b** with carbon pronucleophiles was next examined. Reaction of **28b** with methyl lithium in ether at −78 °C without gold(I) catalyst gave a secondary benzylamine chromium complex **31a** and the diastereomer in a ratio of 92: 8 in 78% yield (Table 7). Treatment of **31a** with PPh_3AuNTf_2 in CH_2Cl_2 at room temperature afforded 1-*syn*-methyl 1,2-dihydroisoquinoline chromium complex **32a** in 86% yield. Similarly, ketene silylacetal was reacted with **28b** in the presence of gold catalyst at room temperature to give a sigle diastereomeric addition product **31b** in 56% yield. The obtained



Scheme 6. Mechanism under basic conditions.

Table 6
Synthesis of 1-*anti*-functionalized 1,2-dihydroisoquinoline chromium complexes.



Entry	Nucleophile (Nu^-)	Lewis acid	Nu	Yield (%)
1	Me_3Al	–	Me	**30a** (67)
2	$CH_2{=}C(OSiMe_3)OEt$	$TiCl_4$	CH_2CO_2Et	**30b** (71)
3	$CH_2{=}CHCH_2Sn^nBu_3$	$BF_3{\cdot}OEt_2$	$CH_2CH{=}CH_2$	**30c** (84)
4	Et_2AlCN	–	CN	**30d** (43)
5	Et_2Zn	$TiCl_4$	Et	**30e** (54)

benzylamine chromium complex **31b** was converted to 1-*syn*-ethoxycarbonylmethyl 1,2-dihydroisoquinoline chromium complex **32b** by further treatment with gold catalyst. However, gold(I)-catalyzed reaction with allyl *n*-tributylstanane at room temperature produced a mixture of the addition product **31c** and 1-*anti*-allyl-1,2-dihydroisoquinoline chromium complex **30c** in 72% and 17% yields, respectively. Under the reaction condition at 0 °C, the yield of cyclized 1-*anti*-allyl-1,2-dihydroisoquinoline chromium complex **30c** decreased (entry 4). The obtained allyl benzylamine chromium complex **31c** afforded 1-*syn*-allyl-2-tosyl-3-methyl-isoquinoline chromium complex (**32c**) in good yield by treatment with the gold catalyst. The stereochemistry of 1-*syn*-substituted 1,2-dihydroisoquinoline chromium complex **32b** was confirmed by X-ray crystallography (Fig. 2) [12]. Interestingly, the arene ring of tosyl group of **32b** is stacking with the chromium-coordinated arene ring with slightly incline, and N–S bond of the tosyl group is oriented as an *anti*-conformation to the tricarbonylchromium fragment to avoid a nonbonding interaction with *syn*-oriented ethyl acetate group. Therefore, 1-*anti*-functinalized 1,2-dihydroisoquinoline chromium complexes **30** and the corresponding *syn*-isomers **32** can be distinguished by proton NMR spectra. Thus, the aromatic protons of tosyl group of *syn*-isomers appear at higher field (δ 7.45 and 7.06 ppm for **32b**) than those (δ 7.88 and 7.34 ppm for **30b**) of the corresponding *anti*-isomer.

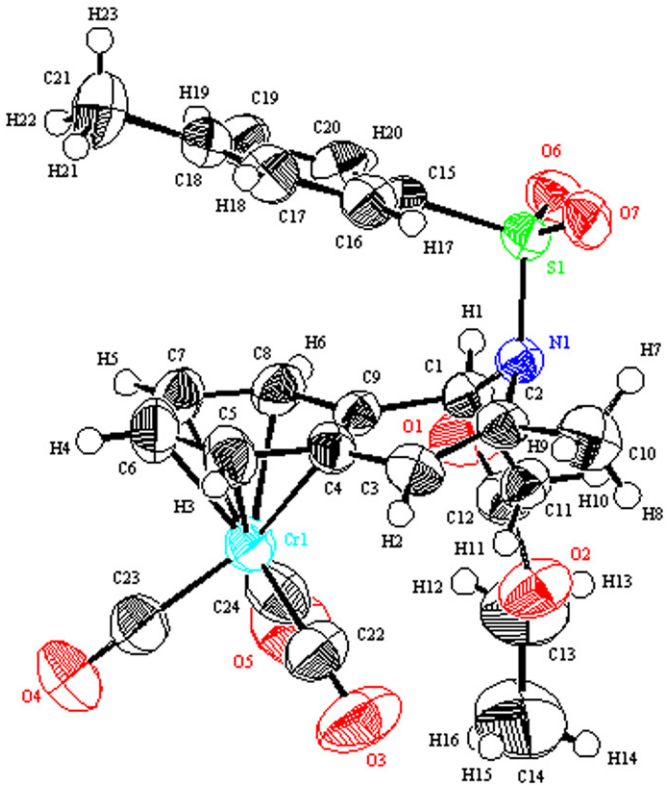


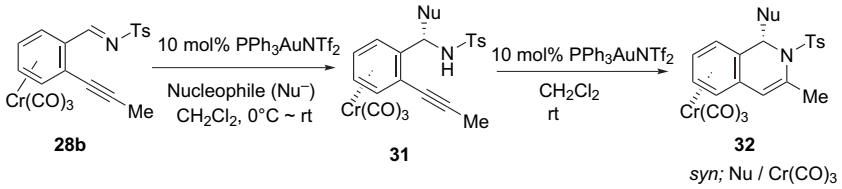
Fig. 2. X-ray crystallography of **32b**.

The formation of 1-*anti*-functionalized-1,2-dihydroisoquinoline chromium complex **30** by gold(I)-catalyzed reaction of **28b** with allyl stannane is quite interesting, since the reaction of **28b** with other carbon nucleophiles gave 1-*syn*-functionalized 1,2-dihydroisoquinoline chromium complexes *via* stereoselective addition products of nucleophiles to the imine double bond in analogy with the reaction of *o*-alkynyl benzaldehyde chromium complexes with carbon nucleophiles as shown in Table 3. The reaction mechanism for the *anti*-isomer of 1,2-dihydroisoquinoline chromium complex **30** from the chromium complex **28b** is follows. Nucleophilic ability of the addition of employing reagents to the imine bond would govern the reaction products. The addition of allyl tributylstannane to the imine and generation of chromium-complexed isoquinolinium ion take place competitively. As the nucleophilicity of the allyl stannane to the imine double bond is not so strong, the generated chromium-complexed isoquinolinium ion intermediate would be attacked a part by the allyl group from *exo*-side giving 1-*anti*-allyl-1,2-dihydroisoquinoline chromium complex **30c**. On the other hand, 1-*syn*-allyl-1,2-dihydroisoquinoline chromium complex **32c** was formed *via* stereoselective addition of the allyl to imine double bond.

3. Conclusion

Gold(I)-catalyzed cyclization of *o*-alkynyl benzaldehyde and benzaldimine chromium complexes gave stereoselectively 1-*anti*- and *syn*-functionalized heterocycle chromium complexes depending on the nature of nucleophiles. With alcohol nucleophiles, 1-*anti*-alkoxy-heterocycle chromium complexes were stereoselectively obtained *via* gold benzopyrylium-type intermediates, while carbon pronucleophiles gave 1-*syn*-functionalized heterocycle chromium complexes *via* stereoselective addition of nucleophiles to the activated carbon-heteroatom double bond and subsequent cyclization. By using these methods, enantiomerically pure *trans*- and both enantiomers of *cis*-1,3-dimethylisochromans were stereoselectively prepared starting from planar chiral *o*-chrorobenzaldehyde tricarbonylchromium complex.

Table 7
Synthesis of 1-*syn*-functionalized 1,2-dihydroisoquinoline chromium complexes.



28b **31** **32**

syn; Nu / $Cr(CO)_3$

Entry	Nu–	Nu	Yield of **31** (%)	Yield **32**
1[a]	MeLi	Me	**31a** (78)	**32a** (86)
2[b]	CH_2=C($OSiMe_3$)OEt	CH_2CO_2Et	**31b** (56)	**32b** (68)
3[b]	CH_2=$CHCH_2Sn(n\text{-}Bu)_3$	CH_2CH=CH_2	**31c** (72), **30c** (15)	**32c** (86)
4[c]	CH_2=$CHCH_2Sn(n\text{-}Bu)_3$	CH_2CH=CH_2	**31c** (69), **30c** (3)	–

[a] Reaction took place in ether at −78 °C without gold catalyst.
[b] rt, 2 h.
[c] 0 °C, 3 h.

4. Experimental

4.1. General comments

All manipulations involving organometallics were carried out under an atmosphere of argon or nitrogen with inert gas/vacuum double-manifold techniques. Diethyl ether and tetrahydrofuran were distilled from sodium/benzophenone ketyl immediately before use. Methylene chloride was distilled over P_2O_5 before use. Melting points were determined by Yanaco MP micro melting apparatus and were uncorrected. NMR spectra were recorded in $CDCl_3$ solvent with tetramethylsilane as an internal reference on JNM-AL-300 (300 MHz) or Varian Unity Inova (400 MHz). IR spectra were recorded as a solution in $CHCl_3$ with a JASCO Fourier Transform Spectrometer. Mass spectra were recorded on JEOL GC mate instruments with EI mode. Optical rotations were measured on a JASCO DIP-360 automatic polarimeter at 589 nm (sodium D line) using a 0.5 dm cell.

4.2. General procedure of gold(I)-catalyzed reaction of o-alkynyl benzaldehyde chromium complexes with alcohols. Preparation of (1-anti-methoxy-3-methyl-1H-isochromene)tricarbonylchromium ***5aa***

To a mixture of chromium complex **3a** (250 mg, 0.89 mmol) and PPh_3AuNTf_2 (33 mg, 44.6 μmol) in CH_2Cl_2 (9 mL) was added MeOH (0.18 mL, 4.46 mmol) by a syringe at room temperature under nitrogen, and the reaction mixture was stirred for 30 min. Filtration through a layer of celite, wash with ether, concentration of the organic layer under vacuum and purification by silica gel column chromatography with ether/hexane gave chromium complex **5aa** as yellow crystals. 80% yield. M.p. 85–86 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.62 (1H, s), 5.47 (1H, t, J = 6.2 Hz), 5.46 (1H, d, J = 6.2 Hz), 5.41 (1H, s), 5.17 (1H, d, J = 6.2 Hz), 5.08 (1H, t, J = 6.2 Hz), 3.56 (3H, s), 2.03 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 232.8, 155.2, 103.3, 98.1, 96.6, 96.5, 94.1, 91.1, 88.3, 86.2, 55.9, 19.9. IR ($CHCl_3$) 1969, 1898 cm^{-1}. Anal. Calcd for $C_{14}H_{12}O_5Cr$: C, 53.85; H, 3.87. Found. C, 53.67; H, 3.92.

4.3. [1-(2-(Prop-1-ynyl)phenyl)]but-3-en-1-ol] tricarbonylchromium ***8a***

Method A: (reaction with PPh_3AuNTf_2): A solution of chromium complex **3a** (50 mg, 0.18 mmol) and Ph_3AuNTf_2 (13 mg, 0.018 mmol) in CH_2Cl_2 (3 mL) was degassed and cooled to −20 °C. Allyl tri-*n*-butylstannane (0.28 mL, 0.89 mmol) was added with syringe, and the mixture was stirred for 1 h at −20 °C. Saturated aqueous KF was added and the reaction mixture was extracted with ether. The ether was washed with saturated aqueous KF, brine and dried over $MgSO_4$. The organic layer was evaporated under vacuum, and purified by SiO_2 column chromatography to give the title compound as yellow crystals in 73% yield.

Method B (reaction with $BF_3{\cdot}OEt_2$): To a mixture of chromium complex **3a** (50 mg, 0.18 mmol) and allyl tri-*n*-butylstannane (0.28 mL, 0.89 mmol) in CH_2Cl_2 (5 mL) was added $BF_3{\cdot}OEt_2$ (44 μL, 0.36 mmol) at −78 °C under nitrogen. The reaction mixture was stirred for 1 h and quenched with aqueous $NaHCO_3$ and extracted with ether. Usual workup gave the title compound in 60% yield. M.p. 79–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84–5.98 (1H, m), 5.62 (1H, d, J = 6.4 Hz), 5.47 (1H, d, J = 6.4 Hz), 5.32 (1H, t, J = 6.4 Hz), 5.28 (1H, t, J = 6.4 Hz), 5.11–5.17 (2H, m), 4.85–4.90 (1H, m), 2.61–2.66 (1H, m), 2.32–2.42 (1H, m), 2.05 (3H, s), 1.55 (1H, brs). IR ($CHCl_3$) 3458, 1971, 1896 cm^{-1}. Anal. Calcd for $C_{16}H_{14}CrO_4$: C, 59.63; H, 4.38. Found. C, 59.50; H, 4.59.

4.4. (1-syn-Allyl-3-methyl-1H-isochromene)tricarbonylchromium ***9a***

A mixture of chromium complex **8a** (50 mg, 0.16 mmol) and PPh_3AuNTf_2 (11 mg, 0.016 mmol) in CH_2Cl_2 (1 mL) was stirred for 2 h at room temperature, and the mixture was filtered with celite washed with ether. The organic layer was evaporated under vacuum, and purified with SiO_2 column chromatography to give the title compound in 68% yield.yellow crystals; M.p. 68–69 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01–6.08 (1H, m), 5.48 (1H, m), 5.47 (1H, d, J = 6.1 Hz), 5.21–5.29 (2H, m), 5.23 (1H, s), 5.00 (1H, d, J = 6.1 Hz), 4.94 (1H, t, J = 6.1 Hz), 4.89 (1H, t, J = 6.1 Hz), 2.75–2.78 (2H, m), 1.94 (3H, s). IR ($CHCl_3$) 1966, 1893 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_4Cr$: C, 59.63; H, 4.38. Found. C, 59.63; H, 4.38.

4.5. (1-Anti-methyl-3-methyl-1H-isochromene) tricarbonylchromium ***10a***

To a solution of chromium complex **5aa** (430 mg, 1.38 mmol) in methylene chloride (14 mL) was added Me_3Al (2.0 M hexane solution, 3.4 mL, 6.89 mmol) at −78 °C under nitrogen, and the mixture was stirred for 30 min, and warmed to −40 °C over 45 min. The reaction mixture was quenched with aqueous $NaHCO_3$ and extracted with ether. The extract was washed with brine, dried over $MgSO_4$ and evaporated under vacuum. Purification by silica gel

chromatography gave the title compound in 99% yield. yellow crystals; M.p. 119–120 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (1H, t, J = 6.4 Hz), 5.30 (1H, d, J = 6.4 Hz), 5.24 (1H, s), 5.07–5.14 (2H, m), 5.03 (1H, q, J = 6.6 Hz), 1.92 (3H, s), 1.52 (3H, d, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 233.4, 157.3, 103.6, 102.6, 96.2, 92.9, 89.6, 88.9, 86.6, 72.9, 20.4, 20.2. IR ($CHCl_3$) 1965, 1892 cm^{-1}. Anal. Calcd for $C_{14}H_{12}CrO_4$: C, 56.76; H, 4.08. Found. C, 56.47; H, 3.89.

4.6. (1-Anti-allyl-3-methyl-1H-isochromene)tricarbonylchromium **10b**

60% yield; yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77–5.90 (1H, m), 5.37 (1H, t, J = 5.9 Hz), 5.26 (1H, d, J = 5.9 Hz), 5.20 (1H, s), 5.04–5.16 (4H, m), 4.91 (1H, dd, J = 7.7, 5.9 Hz), 2.66–2.75 (1H, m), 2.41–2.50 (1H, m), 1.91 (3H, s). IR ($CHCl_3$) 1966, 1893 cm^{-1}. EI-MS (70 eV) m/z (relative intensity fragment) 322 (23, M^+), 295 (2, $M^+ - CH{=}CH_2$), 266 (5, $M^+ - 2CO$), 238 (60, $M^+ - 3CO$), 145 (34, $M^+ - Cr(CO)_3{-}OCH{=}CH_2$), 52 (100, Cr); HRMS ($EI^+$) calcd for $C_{16}H_{14}CrO_4$: 322.0297. Found. 322.0301.

4.7. 3H-spiro(isobenzofuran-1,3′-isochroman)tricarbonylchromium **21**

yellow crystals. M.p. 163 °C decomposed. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.53 (4H, m), 5.38 (1H, t, J = 6.2 Hz), 5.35 (1H, d, J = 6.2 Hz), 5.22–5.30 (2H, m), 5.22 (1H, d, J = 13.0 Hz), 5.08 (2H, d, J = 13.0 Hz), 4.52 (1H, d, J = 13.0 Hz), 3.56 (1H, d, J = 16.9 Hz), 2.85 (1H, d, J = 16.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 233.0, 139.6, 139.4, 129.6, 128.1, 122.4, 121.1, 106.6, 105.2, 103.0, 92.3, 91.8, 90.5, 89.2, 72.0, 62.1, 35.1. IR ($CHCl_3$) 1969, 1896 cm^{-1}. Anal. $C_{19}H_{14}O_5Cr$: Calcd for C, 60.97; H, 3.77. Found. C, 60.68; H. 3.78.

4.8. [1-Anti-methoxy-3-methyl-2-tosyl-1,2-dihydroisoquinoline] tricarbonylchromium **29**

87% yield. Yellow crystals. M.p. 159 °C decomposed. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.88 (2H, d, J = 8.3 Hz), 7.34 (2H, d, J = 8.3 Hz), 6.28 (1H, s), 5.65 (1H, d, J = 6.4 Hz), 5.60 (1H, t, J = 6.4 Hz), 5.57 (1H, s), 5.26 (1H, d, J = 6.4 Hz), 5.05 (1H, t, J = 6.4 Hz), 3.51 (3H, s), 2.41 (3H, s), 2.23 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 232.4, 144.9, 138.2, 136.3, 130.1 (2C), 127.8 (2C), 103.2, 103.2, 100.6, 95.3, 93.0, 86.9, 85.4, 84.6, 54.9, 22.5, 21.6. IR ($CHCl_3$) 1970, 1901 cm^{-1}. Anal. Calcd for $C_{21}H_{19}NO_6SCr$: C, 54.19; H, 4.11; N, 3.01. Found. C, 54.01; H, 4.19; N, 2.96.

4.9. [1-Anti-methyl-3-methyl-2-tosyl-1,2-dihydroisoquinoline] tricarbonylchromium **30a**

yellow crystals; M.p. 161–162 °C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.88 (2H, d, J = 8.3 Hz), 7.33 (2H, d, J = 8.3 Hz), 5.51 (1H, t, J = 6.2 Hz), 5.41 (1H, d, J = 6.2 Hz), 5.38 (1H, s), 5.31 (1H, q, J = 6.7 Hz), 5.00 (1H, d, J = 6.2 Hz), 4.94 (1H, t, J = 6.2 Hz), 2.42 (3H, s), 2.19 (3H, s), 1.46 (3H, d, J = 6.7 Hz). IR ($CHCl_3$) 1968, 1897 cm^{-1}; Anal. Calcd for $C_{21}H_{19}NO_5SCr$: C, 56.12; H, 4.26; N, 3.12. Found. C, 56.35; H, 4.34; N, 3.15.

4.10. [1-Anti-allyl-3-methyl-2-tosyl-1,2-dihydroisoquinoline] tricarbonylchromium **30c**

59% yield. yellow crystals. M.p. 154–155 °C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.88 (2H, d, J = 8.2 Hz), 7.33(2H, d, J = 8.2 Hz), 5.76 (1H, ddt, J = 16.4, 9.9, 6.8 Hz), 5.53 (1H, t, J = 6.4 Hz), 5.41 (1H, d, J = 6.4 Hz), 5.38 (1H, s), 5.24 (1H, t, J = 6.8 Hz), 5.10 (1H, d, J = 9.9 Hz), 5.02 (1H, d, J = 16.4 Hz), 4.98 (1H, d, J = 6.4 Hz), 4.91 (1H, t, J = 6.4 Hz), 2.51 (2H, dd, J = 6.8, 6.8 Hz), 2.41 (3H, s), 2.18 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 232.9, 144.4, 139.8, 137.3, 132.2, 130.0 (2C), 127.6 (2C), 119.7, 106.0, 104.8, 103.2, 95.3, 93.2, 85.6, 84.8, 58.6, 41.3, 22.8, 21.6. IR ($CHCl_3$) 1968, 1898 cm^{-1}; Anal. Calcd for $C_{23}H_{21}NO_5SCr$: C, 58.10; H, 4.45; N, 2.95. Found. C, 58.05; H, 4.26; N, 2.94.

4.11. [Ethyl-3-(p-toluenesulfonamido)-3-(2-(prop-1-ynyl) propanoate)]tricarbonylchromium **31b**

yellow crystals. M.p. 141–142 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (2H, d, J = 8.1 Hz), 7.29 (2H, d, J = 8.1 Hz), 5.97 (1H, d, J = 9.9 Hz), 5.51 (1H, dd, J = 6.4, 1.1 Hz), 5.31 (1H, ddd, J = 6.4, 6.4, 1.1 Hz), 5.19 (1H, dd, J = 6.4, 1.1 Hz), 5.03 (1H, ddd, J = 6.4, 6.4, 1.1 Hz), 4.72 (1H, ddd, J = 9.9, 4.9, 4.9 Hz), 3.99–4.10 (2H,m), 3.12 (1H, dd, J = 16.9, 7.2 Hz), 2.97 (1H, dd, J = 16.9, 7.2 Hz), 2.41 (3H, s), 2.08 (3H, s), 1.19 (3H, t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 231.5, 170.8, 143.9, 136.9, 129.7 (2C), 127.4 (2C), 109.9, 92.8, 92.6, 92.5, 91.2, 87.2, 74.0, 69.8, 61.1, 51.7, 40.2, 21.5, 14.0, 4.5. IR ($CHCl_3$) 1976, 1910, 1719 cm^{-1}. EI-MS (15 eV) m/z (relative intensity, fragment) 521 (23, M^+), 465 (3, $M^+ - 2CO$), 437 (15, $M^+ - 3CO$), 385 (2, $M^+ - Cr(CO)_3$), 321 (2, $M^+ - Ts - OEt$), 306 (18, $M^+ - NHTs - OEt$). HRMS (EI^+) Calcd for $C_{24}H_{23}CrNO_7S$: 521.0600; found. 521.0608. Anal. Calcd for $C_{24}H_{23}NO_7SCr$: C, 55.28; H, 4.45; N, 2.69. Found. C, 55.50; H, 4.55; N, 2.72.

4.12. (1-syn-Methyl-3-methyl-2-tosyl-1,2-dihydroisoquinoline) tricarbonylchromium **32a**

Yellow crystals. M.p. 127–128 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.46 (2H, d, J = 7.9 Hz), 7.07 (2H, d, J = 7.9 Hz), 5.95 (1H, s), 5.42 (1H, d, J = 6.4 Hz), 5.22 (1H, t, J = 6.4 Hz), 5.01 (1H, q, J = 7.0 Hz), 4.82 (1H, t, J = 6.4 Hz), 4.60 (1H, d, J = 6.4 Hz), 2.31 (6H, s), 1.45 (3H, d, J = 7.0 Hz). IR ($CHCl_3$) 1968, 1896 cm^{-1}; Anal. Calcd for $C_{21}H_{19}NO_5SCr$: C, 56.12; H, 4.26; N, 3.12. Found. C, 56.27; H, 4.55; N, 2.83.

4.13. [1-syn-(Ethoxycarbonylmethyl)-3-methyl-2-tosyl-1,2-dihydroisoquinoline]tricarbonylchromium **32b**

Yellow crystals. M.p. 161–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (2H, d, J = 8.3 Hz), 7.06 (2H, d, J = 8.3 Hz), 5.98 (1H, s), 5.66 (1H, d, J = 6.2 Hz), 5.41 (1H, dd, J = 7.3, 7.5 Hz), 5.23 (1H, t, J = 6.2 Hz), 4.81 (1H, t, J = 6.2 Hz), 4.57 (1H, d, J = 6.2 Hz), 4.23 (1H, dd, J = 6.8, 14.0 Hz), 4.22 (1H, dd, J = 7.2, 14.0 Hz), 2.86 (1H, dd, J = 7.3, 16.0 Hz), 2.71 (1H, dd, J = 7.5, 16.0 Hz), 2.33 (3H, s), 2.31 (3H, s), 1.32 (3H, dd, J = 6.8, 7.2 Hz). IR ($CHCl_3$) 1970, 1897, 1727 cm^{-1}; Anal. Calcd for $C_{24}H_{23}NO_7SCr$: C, 55.28; H, 4.45; N, 2.69. Found. C, 55.53; H, 4.51; N, 2.67.

Acknowledgments

This work was supported by a Grant-in-Aid for Scientific Research from Ministry of Education, Culture, Sports, Science and Technology, Japan. We thank also the support of COE Foundation of Kyoto Pharmaceutical University.

Appendix A. Supplementary data

CCDC 741238, 741239, 741240, 741214 and 741242 contain the supplementary crystallographic data for **1, 1a, 2a, 2b** and **3b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Appendix. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2010.06.005.

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