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Asymmetric C–H insertion of Rh(II) stabilized carbenoids into acetals: A C–H activation protocol as a Claisen condensation equivalent

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Abstract

The dirhodium tetraprolinate, Rh_2(*S*-DOSP)$_4$ is an efficient catalyst in an enantioselective C–H activation protocol. Rh_2(*S*-DOSP)$_4$ catalyzed decomposition of aryldiazoacetates or vinyldiazoacetates results in the formation of transient rhodium carbenoid intermediates. These intermediates are capable of selectively inserting into the C–H bond of acetals. The resulting products are protected β-keto esters, and so the C–H activation protocol can be considered as strategically equivalent to the Claisen condensation.

Keywords: Rhodium carbenoid; C–H Insertion; C–H activation; Claisen condensation equivalent

1. Introduction

Developing reliable methods for catalytic C–H activation has been a long-term goal in organometallic chemistry. The majority of the published studies on C–H activation have focused on the use of highly reactive metal complexes, which are able to activate the C–H bond via oxidative addition [1–5]. An alternative method for C–H activation is by means of metal carbenoid induced C–H functionalization [6–12]. Efficient and enantioselective carbon hydrogen bond-insertions of carbenoids were long limited to intramolecular reactions, since intermolecular C–H insertions of carbenes or carbenoids were considered to be unselective, producing mixtures of products [8,13,14]. In addition to their lack of selectivity, the intermolecular insertion reactions suffer from competing secondary reactions such as formation of formal carbene dimers [15]. In recent years, however, it has become apparent that the reactivity profile of carbenoids is very dependent on the carbenoid structure [7,16,17] and catalyst system [18,19]. Because of the presence of the donor group (typically vinyl or aryl), carbenoids **2** are much more stabilized than conventional carbenoids, which contain only electron acceptor groups (typically ester, keto, phosphonate, sulfonate, cyano or nitro) [8,20]. Furthermore, if the reactions of these carbenoids are catalyzed by air-, moisture- and heat-stable dirhodium tetraprolinates like Rh_2(*S*-DOSP)$_4$ (**3a**) or Rh_2(*S*-TBSP)$_4$ (**3b**) or the bridged variants Rh_2(*S*-biDOSP)$_2$ (**4a**) or Rh_2(*S*-biTISP)$_2$ (**4b**) (Fig. 1) high asymmetric induction can be obtained routinely [21–23] (Scheme 1).

It has been demonstrated that with donor/acceptor-substituted rhodium carbenoids **2** in conjunction with catalysts **3a**,**b** or **4a**,**b** very efficient chemo- and stereoselective intermolecular C–H functionalization reactions are feasible [7,24]. These reactions can often be seen as complementary carbenoid versions of many of the classic synthetic reactions of organic chemistry. For example, β-hydroxy esters, normally prepared by an aldol reaction are stereoselectively accessible by C–H functionalization α to oxygen. (Eq. (1), Scheme 2) [25–27]. Similarly, β-amino esters, products of a Mannich condensation, are obtained by C–H activation α to nitrogen (Eq. (2), Scheme 2) [28–30]. This approach has been used successfully by the Davies and Winkler groups to gain direct access to *threo*-methylphenidate, the

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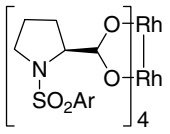

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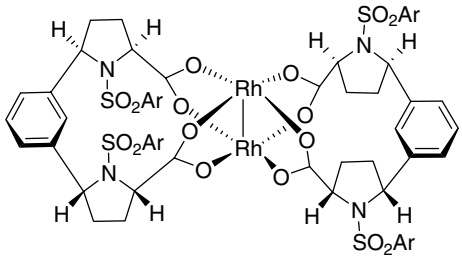
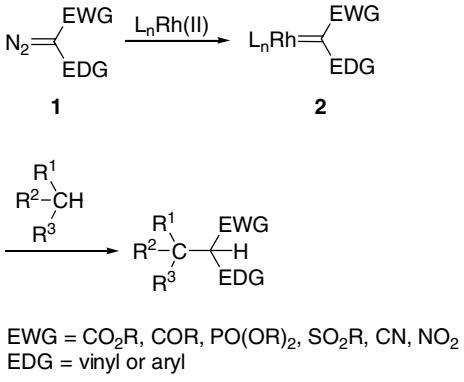
a: Ar = *p*-$C_{12}H_{25}C_6H_4$ Rh_2(S-DOSP)$_4$
b: Ar = *p*-*t*-BuC_6H_4 Rh_2(*S*-TBSP)$_4$



4

a: Ar = *p*-$C_{12}H_{25}C_6H_4$ Rh_2(*S*-biDOSP)$_2$
b: Ar = 2,4,6-*i*-PrC_6H_2 Rh_2(*S*-biTISP)$_2$

Fig. 1.



EWG = CO_2R, COR, $PO(OR)_2$, SO_2R, CN, NO_2
EDG = vinyl or aryl

Scheme 1.

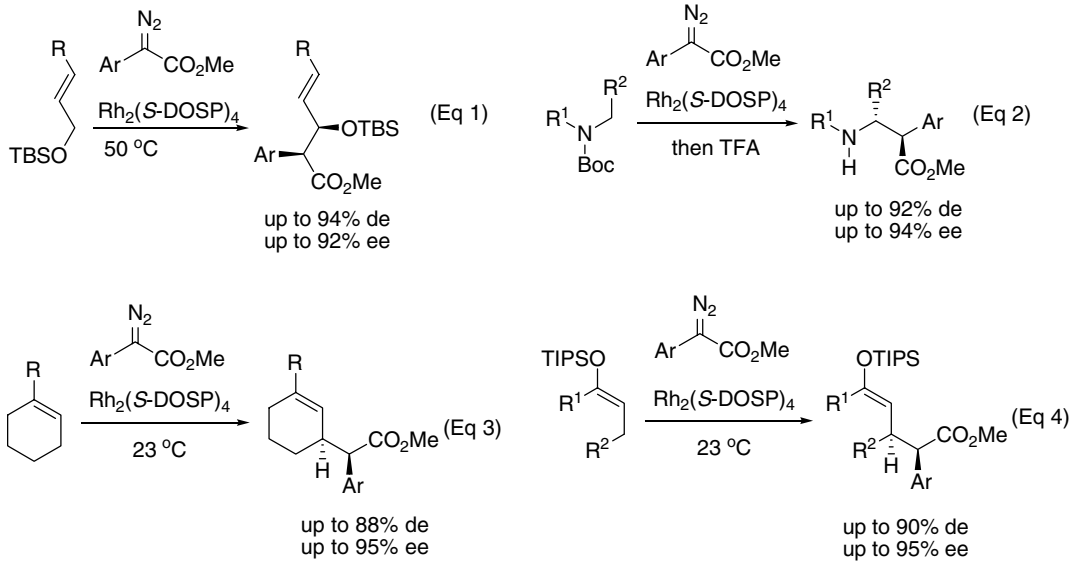
active diastereomer of Ritalin® [28–30]. Allylic C–H activation can lead to γ,δ-unsaturated esters, classically prepared via a Claisen rearrangement (Eq. (3), Scheme 2), or *O*-silylated 1,5-dicarbonyl compounds, the typical products of a Michael addition (Eq. (4), Scheme 2) [31,32].

Besides their very high diastereo- and enantioselectivity, C–H functionalizations with donor/acceptor substituted carbenes **2** show a remarkable chemoselectivity for the site of functionalization. In the same manner as silyl ethers favor C–H functionalization α to oxygen (Eq. (1), Scheme 2), an acetoxy group deactivates this site and C–H functionalization is favored at the allylic site in **5** or the benzylic position, activated by a *p*-methoxyphenyl substituent, in **6** (Scheme 3) [27].

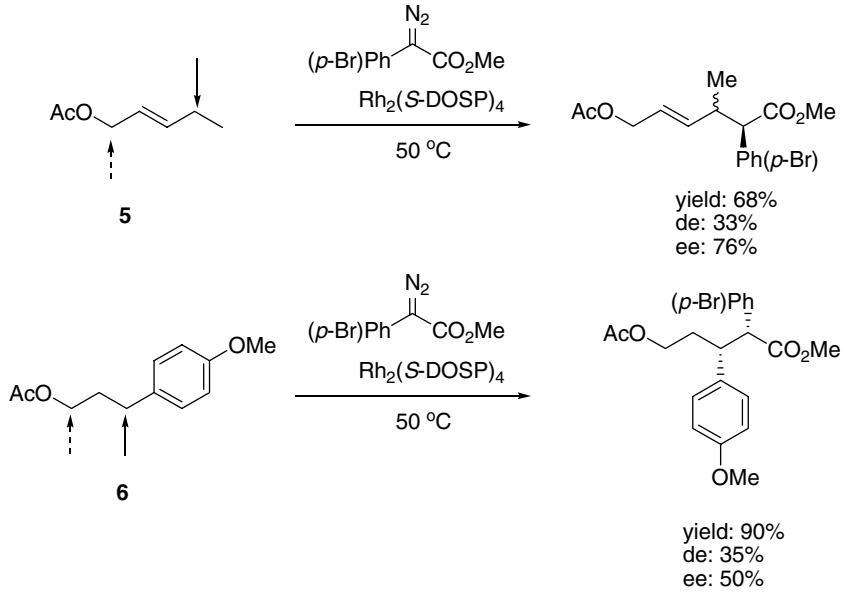
Effects governing the chemoselectivity in C–H functionalizations are subtle: Although it has been established for hydrocarbons that C–H activation at primary sites is least favored [33] and it is known that carbenoids **2** preferentially insert into methylene C–H bonds α to a heteroatom (vide supra), in linear 1,2-dialkoxyalkanes such as **7**, functionalization of the methyl group was observed (Scheme 4). This β oxygen effect is rationalized by inductive deactivation of the methylene sites by the β-oxygen atom [34].

Steric effects at the site of insertion can open alternative reaction pathways to C–H functionalization as is seen in the reaction of cumene (**8**, Scheme 5). Cyclopropanation of the phenyl ring competes with C–H activation at the tertiary site, which is somewhat sterically protected [35].

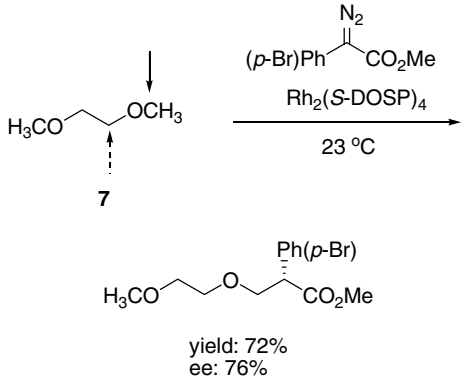
In this article we report the results of our studies into the C–H activation of tertiary sites in acetals to form, chemo- and stereoselectively, ketal-protected β-keto esters (Eq. (5), Scheme 6). This transformation could be considered as a surrogate to the Claisen condensation (Eq. (6), Scheme 6), although it has a major advantage because stereocontrol is unlikely in the standard Claisen condensation due to the epimerizable center in unprotected β-keto esters.



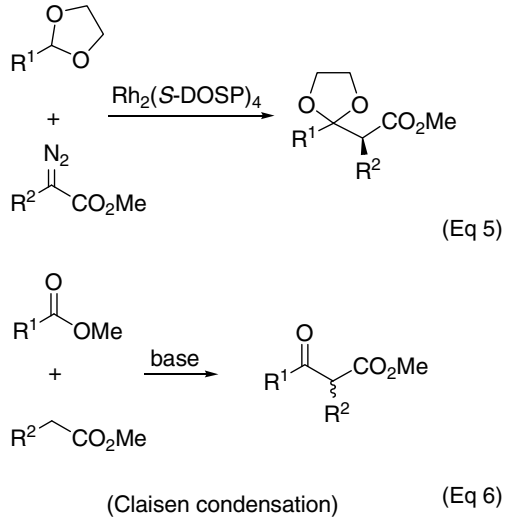
Scheme 2.



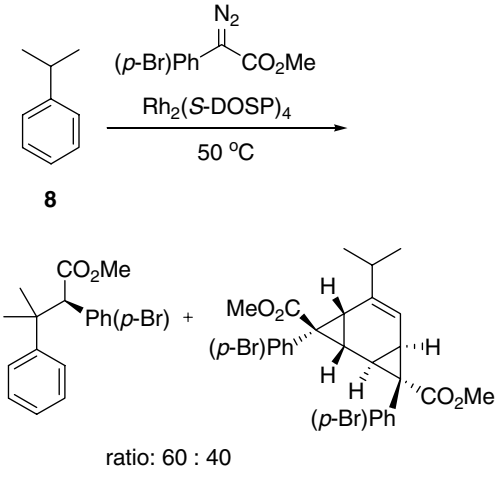
Scheme 3.



Scheme 4.



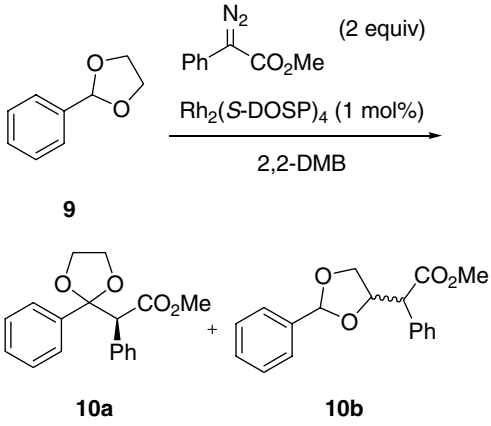
Scheme 6.



Scheme 5.

2. Results and discussion

To explore the possibility of C–H activation of a tertiary center adjacent to heteroatoms, which might activate this site electronically, the reaction of dioxolane **9** was examined (Scheme 7). 2,2-Dimethylbutane (2,2-DMB) was chosen as the solvent because this hydrocarbon solvent is relatively inert towards intermolecular C–H insertion [33]. Interestingly, beside C–H insertion into the sterically hindered acetal C–H bond of **9**, C–H activation at the dioxolane ring was also observed. The C–H insertion products **10a**,**b** were formed in up to 80% combined yield (Scheme 7). The yields did not change whether the reaction was conducted at 50 or −15 °C. However, the use of two equivalents of the phenyldiazoacetate relative to the

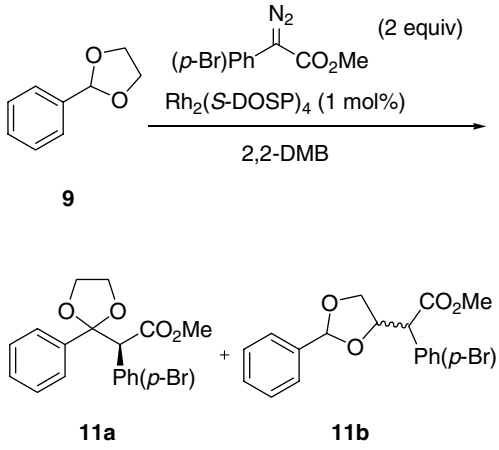


temp. [°C]	yield [%] **10a** + **10b**	ratio[a] **10a**/**10b**	de [%] **10b**[a]
50	76	71:29	30
25	78	74:26	35
-15	80	80:20	50
-30[b]	41	82:18	54

[a]ratio determined from crude proton NMR

[b]conducted with *R*-DOSP. The absolute configuration of the product is opposite to that drawn for **10a**.

Scheme 7.



temp. [°C]	yield [%] **11a** + **11b**	ratio[a] **11a**/**11b**	de [%] **11b**[a]
25	75	89:11	33
-15[b]	79	94:6	53

[a]ratio determined from crude proton NMR

[b]conducted with *R*-DOSP. The absolute configuration of the product is opposite to that drawn for **11a**.

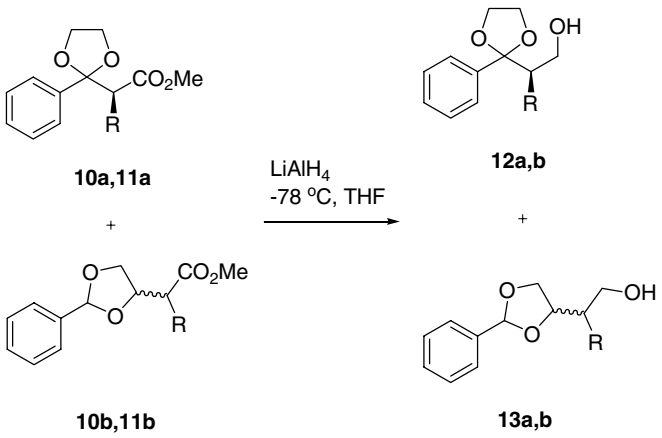
Scheme 8.

substrate was necessary in all cases to ensure good yields. For example, using two equivalents of substrate relative to phenyldiazoacetate resulted in only 42% combined yield of **10a**,**b** for the reaction of **9** catalyzed by Rh_2(*S*-DOSP)$_4$ at 25 °C. The formation of **10a** could be deduced unequivocally from the ^{1}H NMR spectrum showing a distinct singlet at 4.19 ppm, which can be assigned to the proton attached to the newly formed tertiary carbon atom [36]. In contrast, for the minor β-insertion product, the signal for the acetal proton was still found at 5.90 ppm for the major diastereomer and at 5.96 ppm for the minor isomer. The reaction temperature clearly influences the formation of β-insertion product **10b**: lowering the temperature to −30 °C resulted in a 82:18 ratio of **10a** vs. **10b**. At this temperature the de of **10b** also increased to 54% (Scheme 7).

Compared to the carbenoid derived from methyl phenyldiazoacetate, the carbenoid derived from methyl *p*-bromophenyldiazoacetate is more electron deficient and favors more strongly sites that would stabilize positive charge build-up on the carbon of the C–H bond [33]. Therefore, it was not surprising to find greater selectivity in favor of insertion into the acetal C–H bond when using the latter diazo compound as the formation of **11b** is a less favored process due to the aforementioned deactivation of the methylene site by the β-oxygen effect (Scheme 8) [34]. At −15 °C almost exclusive formation of ketal **11a** was observed (Scheme 8). These results suggest that the formation of β-insertion products **10b** and **11b** is a less favorable process due to electronic reasons and becomes less productive at lower temperatures and with more electron deficient carbenoids.

Esters **10** and **11** were inseparable by column chromatography. However, the corresponding alcohols **12a**,**b** and **13a**,**b** could be separated on silica gel and fully characterized. For alcohols **12a** and **13a**, derived from the corresponding C–H insertion products formed at 25 °C, the enantioselectivity was determined to be 61 and 70% ee, respectively (Scheme 9).

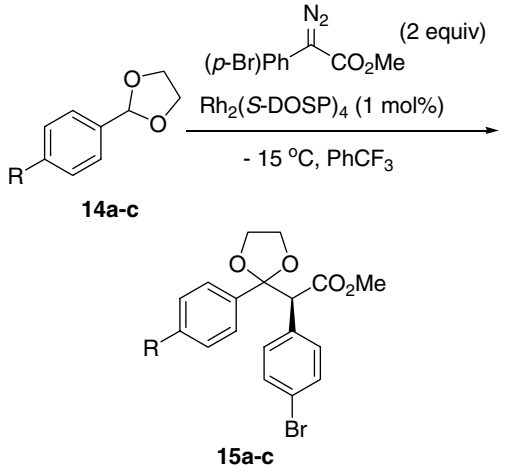
From studies on the C–H insertion of the donor/acceptor substituted carbenoids at benzylic sites, it is known that electron donating substituents in the *para* position greatly enhance the reactivity of benzylic C–H bonds [35]. We consequently examined the reactivity of acetals **14a**–**c** in the reaction with methyl *p*-bromophenyldiazoacetate catalyzed by Rh_2(*S*-DOSP)$_4$ at −15 °C (Scheme 10). At this temperature, 2,2-DMB did not dissolve the employed acetals sufficiently but previous studies had shown that α,α,α-trifluorotoluene ($PhCF_3$) is an adequate replacement for hydrocarbon solvents in Rh_2(*S*-DOSP)$_4$ catalyzed carbene reactions [37]. Under these conditions the desired ketals **15a**–**c** were formed with moderately high asymmetric induction (68–75% ee). No C–H insertion into the dioxolane ring of the acetal was observed. A more significant example of the carbenoid selectivity is the reaction of the



R	12a yield [%]	12a ee [%]	13a yield [%]
Ph	57	61	9

R	12b yield [%]	12b ee [%]	13b yield [%]
(*p*-Br)Ph	76	70	2

Scheme 9.



15	R	yield [%]	ee [%]
a	Br	70	68
b	CH_3	61	70[a]
c	CH_2CH_3	59	75

[a]conducted with *R*-DOSP. The absolute configuration of the product is opposite to taht drawn for **15**.

Scheme 10.

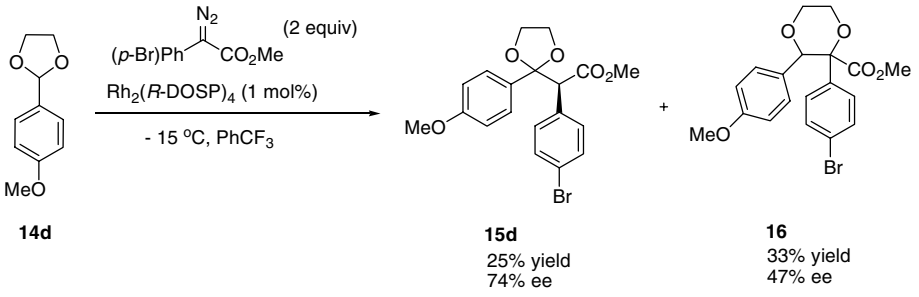
ethyl derivative **14c**, which resulted in only insertion into the ketal C–H bond and no insertion into the benzylic methylene C–H bonds [35].

The reaction of the protected anisaldehyde **14d** led to the formation of a third type of product in addition to the desired ketal. The dioxane **16** was observed beside ketal **15d** (Scheme 11). Compound **16** could be identified unambiguously from its gs-HMBC and gs-HSQC NMR spectra as well as from comparison to published NMR data [38]. The formation of **16** can be rationalized by the intermediate formation of an oxonium ylide formed from the carbenoid with one oxygen atom of the dioxolane ring followed by a [1,2] Stevens-type rearrangement [39,40]. The formation of **16** with 47% ee is noteworthy and suggests that during the ylide formation/rearrangement, the chiral catalyst is not dissociated completely from the ylide and therefore is still able to influence the stereochemical outcome of the rearrangement. The formation of **16** in 47% ee adds a further example to the enantioselective reactions potentially possible by Rh_2(*S*-DOSP)$_4$ (vide infra) [41–45].

An excellent substrate for selective C–H insertion into an acetal was found to be dioxolane **17** derived from cinnamaldehyde. It possesses a phenyl ring that is able to efficiently enhance the C–H insertion event through conjugation (vide supra). At the same time, this bulky group is attached via a sterically less demanding vinyl group to the acetal carbon atom. Initial optimization studies clearly favor Rh_2(*S*-DOSP)$_4$ in $PhCF_3$ at 25 °C (Scheme 12). Under these conditions the C–H insertion product **18a** was formed in 53% yield and 84% ee. Even higher yields could be obtained using 2,2-DMB as solvent but the results were variable due to inhomogeneity of the reaction mixtures. In contrast, using Rh_2(*S*-DOSP)$_4$ in CH_2Cl_2 at 25 °C afforded the C–H insertion product only in 22% yield and 69% ee. Even with the bridged Rh_2(*S*-biTISP)$_2$ catalyst this result could not be improved although it is known that this catalyst is an excellent alternative to Rh_2(*S*-DOSP)$_4$ in cases where CH_2Cl_2 must be used as the solvent [22,29]. In all cases only the desired ketal **18a** was observed and no β-insertion product on the dioxolane ring was detected.

Reactions with various aryldiazoacetates consistently afforded ketals **18b–f** in moderate yields (51–65%). Compared to the ketals derived from dioxolane **9**, the observed enantioinduction was significantly higher for all diazoacetates tested (73–91%) (Scheme 13). We believe that this is due to a sterically less crowded transition state for the C–H insertion which allows for a more efficient catalyst control of the stereochemical outcome of the reaction.

Here, as observed in the benzaldehyde series (vide supra), *para*-methoxy substitution opened a reaction channel leading to the [1,2] rearrangement product **20**. However, in this case, rearrangement product **20** was the major product and was formed as a racemic mixture (Scheme 14). Decreasing enantioselectivity at higher reaction temperatures has been reported in various cases for C–H functionalizations with donor–acceptor substituted carbenoids [27,33,46]. On the other hand, reaction yields tend to be higher at elevated temperatures [27,33,46]. For substrate **19**, it was found that at lower temperatures (0 and −15 °C) the combined yield of **18g**

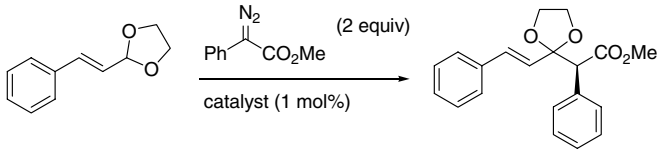


14d

15d
25% yield
74% ee

16
33% yield
47% ee

Scheme 11.

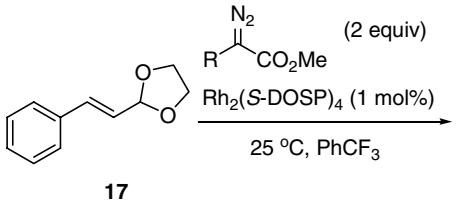


17 **18a**

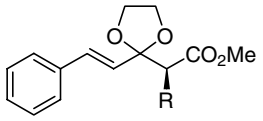
catalyst	temp. [°C]	solvent	yield [%]	ee [%]
Rh_2(*S*-DOSP)$_4$	25	2,2 DMB	up to 60[a]	83
Rh_2(*S*-DOSP)$_4$	50	2,2-DMB	up to 57[a]	78
Rh_2(*S*-DOSP)$_4$	25	CH_2Cl_2	22	69
Rh_2(*S*-DOSP)$_4$	25	$PhCF_3$	53	84
Rh_2(*S*-DOSP)$_4$	103	$PhCF_3$	38	48
Rh_2(*S*-biTISP)$_4$	25	CH_2Cl_2	20	66

[a] yields show considerable variation due to inhomogenous reaction mixture

Scheme 12.



17



18b-f

18	R	yield [%]	ee [%]
b	(*p*-Br)-Ph	65	86
c	(*p*-CH_3)-Ph	57	88
d	(*p*-MeO)-Ph	62	91
e	2-naphthyl	59	73
f	(*p*-Cl)-Ph	51	85[a]

[a]conducted with *R*-DOSP. The abolute configuration of the product is opposite to that drawn for **18**.

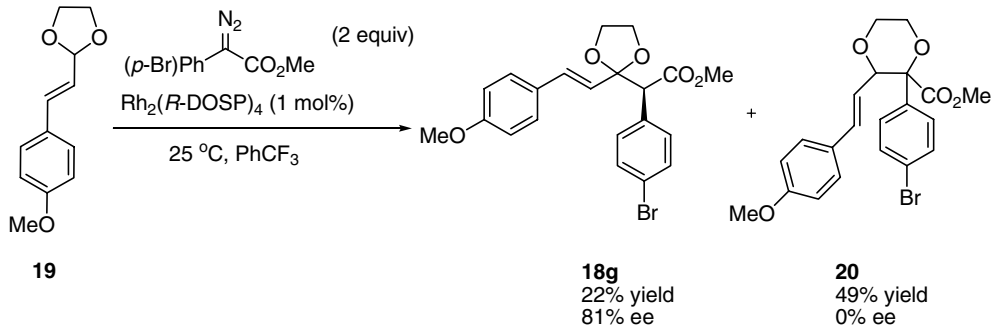
Scheme 13.

and **20** dropped considerably (20–30%) due to significant dimerization of the carbenoid. This result and the finding that dioxolane **16** was formed in 47% ee at −15 °C (Scheme 11) suggest that there is a subtle interplay between substrate structure and reaction conditions which need to be carefully adjusted in order to obtain good yield and stereoselectivity in these [1,2] rearrangement reactions.

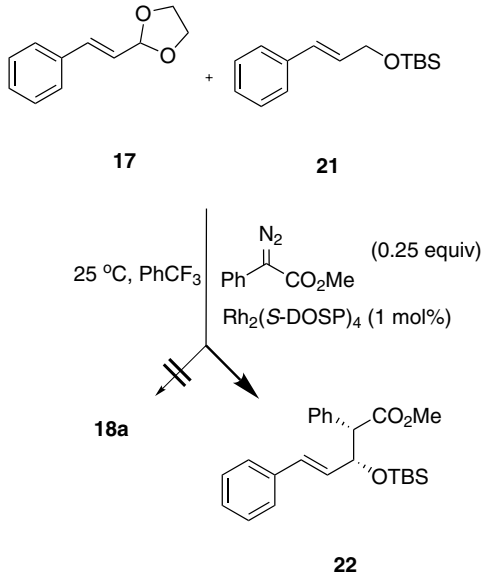
Even though acetals such as **17** would be expected to be electronically highly activated for C–H activation, their overall reactivity behavior suggested that they were not especially favorable substrates. In order to test this, a competition study was conducted between **17** and **21** revealing that the formation of TBS-protected aldol **22** [27] from **21** was considerably favored over formation of acetal **18a**. This result suggests that steric factors are playing a role in decreasing the reactivity of the acetals towards C–H activation. Compound **18a** was not even observed by ESI-MS of the reaction mixture (Scheme 15).

In order to test the steric issues further, the alkyne derivative **23** was prepared. The linear nature of the alkyne would make the acetal C–H bond less sterically encumbered than the other acetal substrates, and thus **23** would be predicted to be a superior substrate in this chemistry. This was indeed the case as the C–H insertion product **24** could be prepared in 68% yield and 86% ee (Scheme 16). Normally, alkynes are prone to cyclopropenation, but the steric demands of the donor/acceptor substituted carbenoids limit cyclopropenation to mono-substituted alkynes [47].

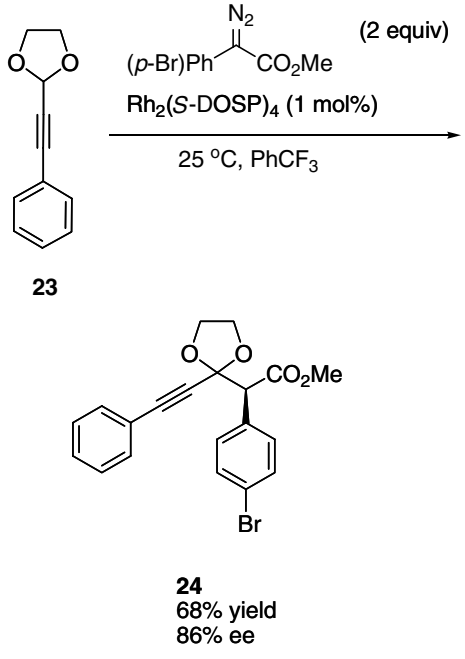
Finally we turned our attention to rhodium(II) carbenoids derived from the decomposition of phenylvinyldiazoacetate (**25**) with Rh_2(*S*-DOSP)$_4$ in the presence of acetal **9** (Scheme 17). Although yields for C–H insertion to form **26** with this carbenoid precursor were lower (42–48%) than the aryldiazoacetates, the enantioselectivity was much higher (80–89% ee). Unlike in the phenyldiazoacetate series no β-insertion product was observed. Again, we explain this selectivity on the basis of the reduced steric demand at the site of C–H activation; this time achieved by reducing the steric demand of the carbenoid center. It should be noted that despite serious attempts, no C–H insertion products were isolated from the reactions of **25**



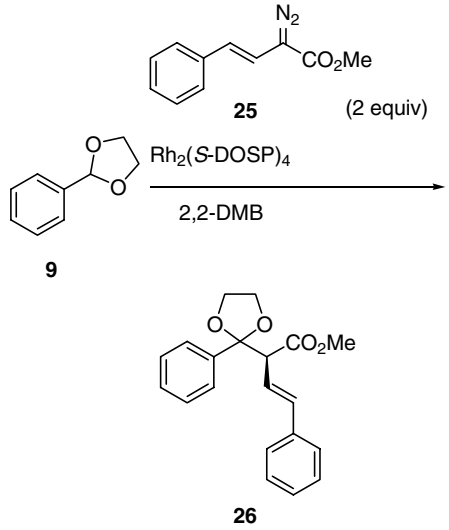
Scheme 14.



Scheme 15.



Scheme 16.

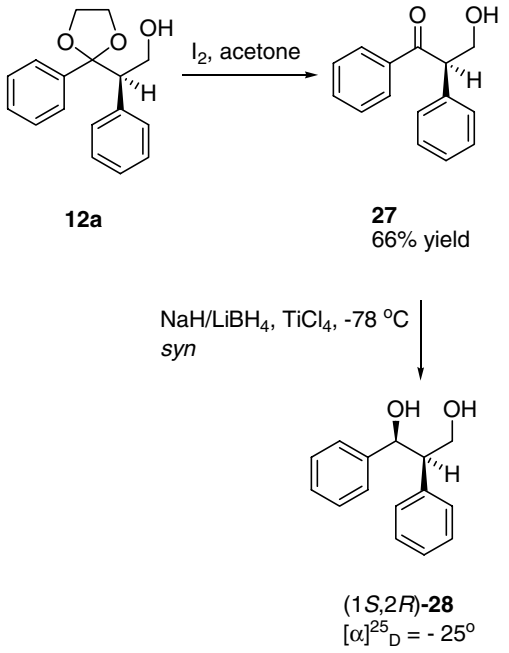


temp. [°C]	catalyst [mol%]	yield [%]	ee [%]
25	2	48	80
25	4	46	89
50	4	42	81

Scheme 17.

with other acetal substrates such as **17** or **19**. As seen previously for the reaction of acetal **9** with phenyldiazoacetates, the use of a twofold excess of the acetal resulted in a considerable drop in yield for the $Rh_2(S\text{-DOSP})_4$ catalyzed reaction of **9** with **25** (only 22% isolated yield).

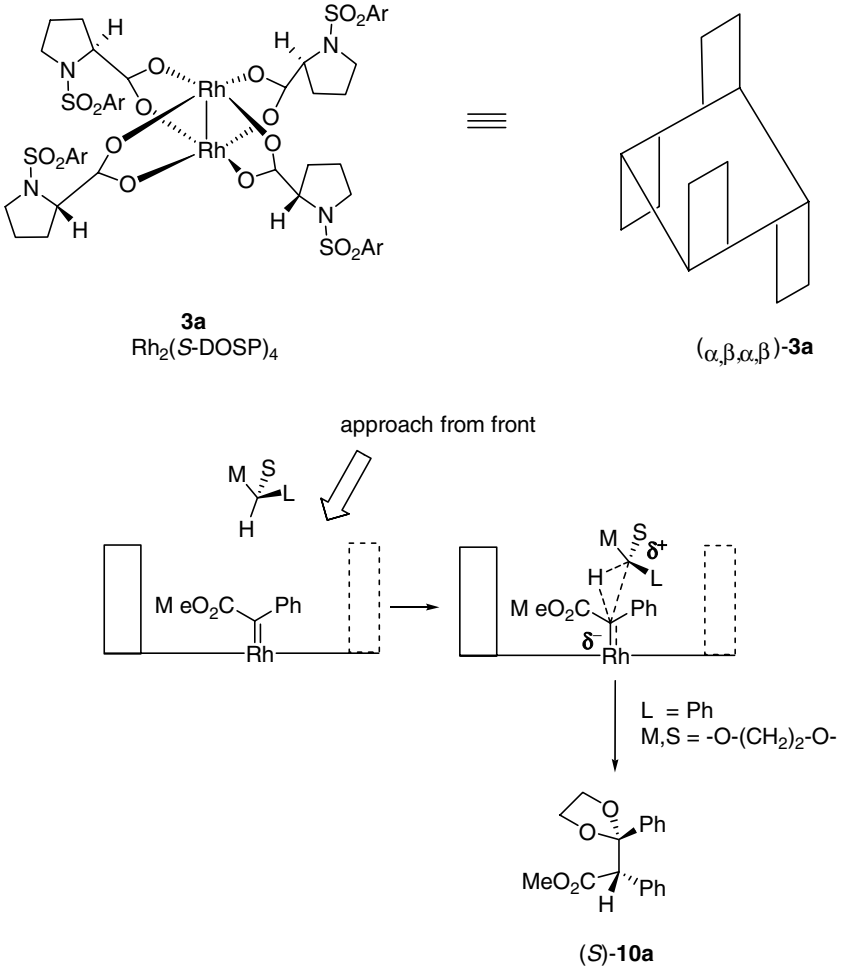
The absolute configuration of the stereocenter created in the C–H insertion reaction was deduced from diol **28**. Diol **28** was prepared from **12a** by hydrolysis of the ketal [48] followed by *syn* reduction [49] of the resulting ketone **27** (Scheme 18). In an independent study, the absolute stereochemistry of diol **28** has been assigned as (1*R*,2*S*) with $[\alpha]_D^{25} = 45$ [50]. Comparing the respective specific optical rotations of diol **28** from that study and **28** prepared in this work, the asymmetric carbon in **10a** could be assigned as (*S*). The stereochemistry of the other C–H activation products is tentatively assigned assuming a similar trajectory of approach of the substrate leading to the same sense of asymmetric induction.



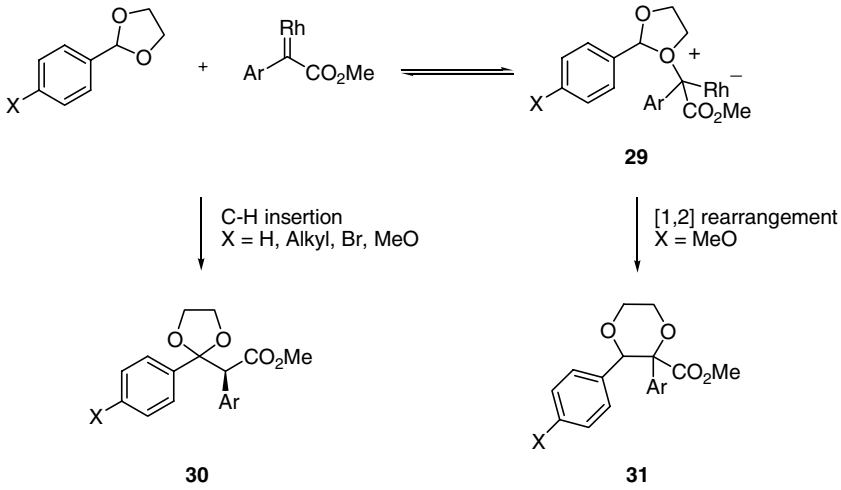
Scheme 18.

The stereochemical result emphasizes once again the high predictability of the C–H insertion process catalyzed by Rh_2(S-DOSP)$_4$. Based on the model developed in our group [16,17,21,51] (Scheme 19), approach of the substrate from the front to the carbene coordinated to the chiral Rh(II) catalyst, an (*S*) configuration of the formed asymmetric carbon atom would be expected. In the predictive model shown in Scheme 19 the D_2 symmetric Rh_2(*S*-DOSP)$_4$ is assumed to have an α,β,α,β conformation [23] to which the carbene is bound in the manner shown allowing for only one defined approach of the substrate.

This study demonstrates the subtle interplay between steric and electronic effects that controls the regioselectivity of the C–H activation chemistry. The acetal site is electronically highly activated but is close to the limit in terms of steric crowding. The best substrate is alkyne **23**, which is the least sterically demanding. Due to the steric crowding, a competing reaction at the C-3 position of the acetal can occur to a small extent even though electronically this is considerably less favored, especially as it contains a β-oxygen group.



Scheme 19.



Scheme 20.

One of the most intriguing aspects of the current study is the observation of the Stevens rearrangement product when the acetal had a methoxy substituent on the aromatic ring. One of the remarkable features of the intermolecular C–H insertion chemistry of the donor/acceptor substituted rhodium carbenoids is that the chemistry is compatible with various mildly nucleophilic sites. The highly electrophilic carbenoids would be expected to be reactive towards nucleophiles and the fact that C–H activation still occurs would suggest that the reaction of these stabilized carbenoids with weak nucleophiles to form an ylide like **29** might be reversible. In this case the presence of the methoxyphenyl substituent would not influence the ability of the acetal to react with the carbenoid to form an ylide, but once ylide **29** is formed the methoxyphenyl group would be expected to enhance the [1,2] rearrangement to dioxane **31** (Scheme 20) [52]. It is thus tempting to speculate that all the acetals are forming ylides but this is an unproductive step and probably reversible except in the case of the methoxyphenyl derivative.

In summary, we have shown that chemo- and stereoselective C–H activation of tertiary C–H bonds with donor/acceptor carbenoids is in fact a feasible and predictable process if the C–H bond is (a) electronically sufficiently activated as in dioxolanes which have either an aryl or vinyl aryl substituent attached to the site of C–H insertion and/or (b) the site of C–H activation is not too crowded. Steric hindrance can be avoided either by using sterically less crowded substrates or carbenoids derived from phenylvinyldiazoacetates.

3. Experimental

All reactions sensitive to air and moisture were carried out in rigorously dried glassware under an Ar atmosphere. 2,2-Dimethylbutane (2,2-DMB) was distilled from Na under argon. CH_2Cl_2 was dried by passage through a solvent purification system packed with Al_2O_3. Purchased α,α,α-trifluorotoluene ($PhCF_3$) had purity $>99\%$ and was degassed prior to use. NMR spectra were recorded at 293 K at 400 or 500 MHz for ^1H and 75 or 125 MHz for ^{13}C. All ^{13}C NMR spectra were recorded ^1H decoupled. TMS ($\delta = 0.0$) served as internal standard for ^1H NMR spectra and $CDCl_3$ ($\delta = 77.0$) for ^{13}C. Assignments of ^{13}C chemical shifts were based on DEPT 135 experiments. IR spectra were recording on a FT-IR instrument using an ATR unit (diamond crystal) for oils and as KBr pellets for solids. Melting points are uncorrected (heating rate 2 °C/min). Analytical TLC was performed on 0.25 mm E. Merck silica gel (60F-254) plates. Phosphomolybdic acid (PMA) in ethanol was used as visualizing reagent to detect compounds with no or only weak UV absorbtion at 254 nm. Flash column chromatography was performed on silica gel 60A (230–400 mesh). Enantiomeric excess (ee) was determined by HPLC with UV detection using isopropanol/hexanes as eluent.

Starting materials. All diazo compounds were prepared analogously to published procedures [53] and gave satisfactory spectroscopic data. Acetals **14a**,**b**, **17** and **19** were prepared following Noyori's protocol [54]. Acetal **23** was prepared as published [55]. Detailed spectroscopic data for **14c** are reported here, since they have not yet been reported.

3.1. 2-(4-Ethylphenyl)-1,3-dioxolane (*14c*)

Preparation from 4-ethylbenzaldehyde and 1,2-bis(trimethylsiloxy)ethane according to the literature [54]; colorless oil, b.p. 100 °C/5 mbar. IR (film): $\nu = 2964$ (m), 2877 (m), 1080 (s), 966 (m), 941 (m), 825 (s) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 1.22$ (t, $J = 7.3$ Hz, 3H), 2.65 (q, $J = 7.3$ Hz, 2H), 4.00–4.04 (m, 2H), 4.10–4.14 (m, 2H), 5.78 (s, 1H), 7.20 (d, $J = 8.1$ Hz, 2H), 7.38 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 15.5$ (CH_3), 28.6, 65.2 (both CH_2), 103.7, 126.4, 127.8 (all CH), 135.1, 145.4 (both C). HRMS (EI): Calc. $C_{11}H_{14}O_2$ 178.0994; found 177.0912 [M^+-1].

3.2. (S)-Methyl 2-phenyl-2-(2-phenyl-1,3-dioxolan-2-yl)acetate (**10a**) and methyl 2-phenyl-2-(2-phenyl-1,3-dioxolan-4-yl)acetate (**10b**)

To a stirred solution of **9** (0.17 g, 1.1 mmol) and Rh_2(*S*-DOSP)$_4$ (42 mg, 0.022 mmol) in 2,2-DMB (5 ml) at 25 °C was added methyl 2-diazophenylacetate (0.39 g, 2.2 mmol) in 2,2-DMB (10 ml) via a syringe pump over 2 h. The reaction mixture was stirred at 25 °C for 1 h and then concentrated in vacuo. The crude product was purified via column chromatography (petroleum ether/diethyl ether 5:1) to afford an inseparable mixture of **10a** and **10b** (0.25 g, 78%) as colorless oil; $R_f = 0.52$. From the ^{1}H NMR spectrum of the crude reaction mixture the ratio of **10a**:**10b** was determined as 74:26; de for **10b** 35%. **10a**: ^{1}H NMR ($CDCl_3$): $\delta = 3.58$ (s, 3H), 3.72–3.79 (m, 2H), 3.84–3.93 (m, 2H), 4.19 (s, 1H), 7.23–7.25 (m, 6H), 7.30–7.32 (m, 2H), 7.37–7.38 (m, 2H). Compare also the literature [36]. ^{13}C NMR ($CDCl_3$): $\delta = 51.8$ (CH_3), 60.5 (CH), 64.9, 65.3 (both, CH_2), 109.4 (C), 126.3, 127.5, 127.6, 127.7, 128.1, 130.3 (all CH), 133.5, 140.8, 170.4 (all C). Compound **10b** was characterized as the corresponding alcohol **13a**.

3.3. (S)-Methyl 2-(4-bromophenyl)-2-(2-phenyl-1,3-dioxolan-2-yl)acetate (**11a**) and methyl 2-(4-bromophenyl)-2-(2-phenyl-1,3-dioxolan-2-yl)acetate (**11b**)

From **9** (0.05 g, 0.36 mmol) and Rh_2(*R*-DOSP)$_4$ (13 mg, 0.007 mmol) in 2,2-DMB (5 ml) and methyl 2-diazo-(4-bromophenyl)acetate (0.18 g, 0.73 mmol) in 2,2-DMB (10 ml). Yield: 0.10 g (75%), colorless oil; $R_f = 0.43$ (petroleum ether/diethyl ether 5:1). From the ^{1}H NMR spectrum of the crude reaction mixture the ratio of **11a**:**11b** was determined as 89:11; de for **11b** 33%. **11a**: ^{1}H NMR ($CDCl_3$): $\delta = 3.58$ (s, 3H), 3.72–3.80 (m, 2H), 3.85–3.93 (m, 2H), 4.15 (s, 1H), 7.25–7.27 (m, 5H), 7.30–7.32 (m, 2H), 7.35–7.37 (m, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 51.9$ (CH_3), 59.9 (CH), 64.9, 65.3 (both CH_2), 109.1, 121.9 (both C), 126.2, 127.8, 128.2, 130.9, 132.1 (all CH), 132.5, 140.5, 170.0 (all C). Compound **11b** was characterized as the corresponding alcohol **13b**.

3.4. (R)-2-Phenyl-2-(2-phenyl-1,3-dioxolan-2-yl)ethanol (**12a**) and 2-phenyl-2-(2-phenyl-1,3-dioxolan-4-yl)ethanol (**13a**)

To a solution of $LiAlH_4$ (1.42 ml, 1 M in THF) in THF (5 ml) at −78 °C was added dropwise **10a**,**b** dissolved in THF (10 ml). The reaction mixture was stirred for 15 min at this temperature and then for 2.5 h at 0 °C. The reaction mixture was quenched at 0 °C by successive additions of water (55 μl), 4 N NaOH (55 μl) and water (160 μl) [56]. The white precipitate was removed by filtration and washed with diethyl ether (50 ml). Removal of the solvent afforded a colorless oil that was further purified by column chromatography. **12a**: Yield: 0.22 g (57%), colorless oil; $R_f = 0.47$ (PMA, petroleum ether/diethyl ether 1:4). ee (Regis RR-Whelk 4 × 250 mm, 3% isopropanol in hexane, 1 ml/min, 254 nm): 61% (major: 16.3 min; minor: 19.1 min); **13a**: Yield: 34 mg (9%), colorless oil; $R_f = 0.37$ (PMA, petroleum ether/diethyl ether 1:4). Only the major diastereomer of **13a** could be isolated. **12a**: IR (film): $\nu = 3442$ (br), 3063 (w), 3028 (w), 2951 (w), 2891 (w), 1495 (w), 1169 (m), 1026 (s), 955 (m), 764 (m), 698 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 2.78$ (br t, 1H), 3.38 (dd, $J = 7.3$, 5.4 Hz, 1H), 3.65–3.69 (m, 1H), 3.74–3.83 (m, 2H), 3.94–4.03 (m, 2H), 4.18–4.24 (m, 2H), 7.00–7.03 (m, 2H), 7.13–7.19 (m, 8H). ^{13}C NMR ($CDCl_3$): $\delta = 56.6$ (CH), 63.3, 63.9, 64.7 (all CH_2), 111.7 (C), 126.2, 126.8, 127.6, 127.7, 127.9, 129.6 (all CH), 137.4, 140.4 (both C). HRMS (ESI): Calc. for $C_{17}H_{18}O_3Na$ 293.1148; found 293.1145. **13a**: IR (film): $\nu = 3410$ (br), 3032 (w), 2883 (w), 1217 (m), 1066 (m), 1026 (m), 758 (m), 696 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 1.73$ (br t, 1H), 3.06 (ddd, $J = 6.6$, 6.6, 6.6 Hz, 1H), 3.67 (dd, $J = 8.0$, 8.0 Hz, 1H), 3.93–4.04 (m, 2H), 4.24 (dd, $J = 8.4$, 6.2 Hz, 1H), 4.60 (ddd, $J = 8.0$, 6.2, 5.5 Hz, 1H), 5.71 (s, 1H), 7.28–7.41 (m, 10H). ^{13}C NMR ($CDCl_3$): $\delta = 50.6$ (CH), 64.5, 68.7 (both CH_2), 76.6 103.8, 126.3, 127.4, 128.3, 128.7, 129.1, 129.2 (all CH), 138.03, 138.3 (both C).

3.5. (R)-2-(4-Bromophenyl)-2-(2-phenyl-1,3-dioxolan-2-yl)ethanol (**12b**) and 2-(4-bromophenyl)-2-(2-phenyl-1,3-dioxolan-4-yl)ethanol (**13b**)

From **11a**,**b** (0.8 g, 2.1 mmol) dissolved in THF (15 ml) and $LiAlH_4$ (2.12 ml, 1 M in THF) in THF (5 ml) at −78 °C. **12b**: Yield: 0.57 g (76%), colorless oil; $R_f = 0.54$ (PMA, petroleum ether/diethyl ether 1:4). ee (Regis RR-Whelk 4 × 250 mm, 5% isopropanol in hexanes, 1 ml/min, 254 nm): 70% (major: 14.8 min; minor: 21.3 min); **13b**: Yield: 11 mg (2%), colorless oil; $R_f = 0.37$ (PMA, petroleum ether/diethyl ether 1:4). Only the major diastereomer of **13b** could be isolated. **12b**: IR (film): $\nu = 3441$ (br), 3061 (w), 2951 (w), 2889 (w), 1489 (m), 1038 (s), 1011 (s), 733 (s), 702 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 2.77$ (br t, 1H), 3.34 (dd, $J = 7.3$, 5.5 Hz, 1H), 3.67 (m, 1), 3.76 (m, 2H), 3.97 (m, 2H), 4.15 (dd, $J = 10.8$, 7.3 Hz, 1H), 5.26 (s, 1H), 6.90 (d, $J = 8.4$ Hz, 2H), 7.18 (m, 5H), 7.27 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 56.0$ (CH), 63.0, 64.0, 64.7 (all CH_2), 111.3, 120.9 (both C), 126.1, 127.8, 128.1, 130.8, 131.3 (all CH), 136.6, 140.2 (both C). HRMS (ESI): Calc. for $C_{17}H_{17}BrO_3Na$ 371.0253; found 371.0255 – Calc. for $C_{17}H_{17}{}^{81}BrO_3Na$ 373.0233; found 373.0241. **13b**: IR (film): $\nu = 3431$ (br), 3032 (w), 2924 (w), 2885 (w), 1489 (m), 1402 (w), 1217 (w), 1070 (s), 1011 (s), 758 (m), 733 (s), 698 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 1.66$ (br t, 1H), 3.01 (ddd, $J = 6.6$, 6.6, 6.6 Hz, 1H), 3.72 (dd, $J = 8.0$, 8.0 Hz, 1H), 3.90–4.00 (m, 2H), 4.25 (dd, $J = 8.4$ Hz, 6.2 Hz, 1H), 4.57 (ddd, $J = 7.7$, 7.7, 5.5 Hz, 1H), 7.21 (d, $J = 8.4$ Hz, 2H), 7.33–7.40 (m, 5H), 7.47 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 50.1$ (CH), 64.4, 68.7 (both CH_2), 76.3, 103.8 (both CH), 121.3 (C), 126.3, 128.3, 129.1, 130.9, 131.9 (all CH), 137.2, 138.1 (both C).

3.6. (S)-Methyl 2-(2-(4-bromophenyl))-2-(2-(4-bromophenyl)-1,3-dioxolan-2-yl)acetate (**15a**)

To a stirred solution of **14a** (0.11 g, 0.49 mmol) and Rh_2(*S*-DOSP)$_4$ (19 mg, 0.01 mmol) in $PhCF_3$ (5 ml) at −15 °C was added methyl 2-diazo(4-bromophenyl)acetate (0.25 g, 0.98 mmol) in $PhCF_3$ (5 ml) via a syringe pump over 2 h. The reaction mixture was allowed to warm to 25 °C over night and then concentrated in vacuo. The sticky, green oil was purified via column chromatography (petroleum ether/diethyl ether 5:1) to afford **15a** (0.16 g, 70%) as colorless oil; $R_f = 0.30$ (PMA). ee (Chiralcel OD-H 4 × 250 mm, 1% isopropanol in hexanes, 1 ml/min, 230 nm): 68% (major: 12.3 min; minor: 14.0 min). IR (film): $\nu = 2950$ (w), 2890 (w), 1744 (s), 1488 (m), 1154 (m), 1012 (s), 822 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 3.59$ (s, 3H), 3.70–3.77 (m, 2H), 3.86–3.94 (m, 2H), 4.09 (s, 1H), 7.14–7.18 (m, 2H), 7.23–7.25 (m, 2H), 7.36–7.39 (m, 4H). ^{13}C NMR ($CDCl_3$): $\delta = 52.0$ (CH_3), 59.6 (CH), 65.0, 65.4 (both CH_2), 108.8, 122.1, 122.5 (all C), 128.2, 130.9, 131.0, 131.9 (all CH), 132.1, 139.6, 169.8 (all C). Anal. Calc. for $C_{18}H_{16}Br_2O_4$ (456.12): C, 47.40; H, 3.54. Found: C, 47.34; H, 3.32.

3.7. (S)-Methyl 2-(4-bromophenyl)-2-(2-p-tolyl-1,3-dioxolan-2-yl)acetate (**15b**)

From **14b** (80 mg, 0.49 mmol) and Rh_2(*R*-DOSP)$_4$ (18 mg, 0.01 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(4-bromophenyl)acetate (0.25 g, 0.98 mmol) in $PhCF_3$ (5 ml). Yield: 0.12 g (61%), colorless oil; $R_f = 0.27$ (PMA, petroleum ether/diethyl ether 5:1). ee (Chiralcel OD-H 4 × 250 mm, 1% isopropanol in hexanes, 1 ml/min, 230 nm): 70% (major: 9.5 min; minor: 15.3 min). IR (film): $\nu = 2950$ (w), 2892.8 (w), 1743 (s), 1149 (s), 1010 (s), 817 (m), 763 (m), 736 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 2.31$ (s, 3H), 3.58 (s, 3H), 3.71–3.78 (m, 2H), 3.83–3.91 (m, 2H), 4.14 (s, 1H), 7.06 (d, $J = 8.3$ Hz, 2H), 7.18 (d, $J = 8.3$ Hz, 2H), 7.27 (d, $J = 8.5$ Hz, 2H), 7.36 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 21.0$, 52.5 (both CH_3), 59.8 (CH), 64.8, 65.2 (both CH_2), 109.1, 121.8 (both C), 126.1, 128.4, 130.8, 132.0 (all CH), 132.6, 137.5, 137.8, 170.0 (all C). HRMS (ESI): Calc. for $C_{19}H_{19}BrO_4Na$ 413.0359; found 413.0369 – Calc. for $C_{19}H_{19}{}^{81}BrO_4Na$ 415.0338; found 415.0351.

3.8. (S)-Methyl 2-(4-bromophenyl)-2-(2-(4-ethylphenyl)-1,3-dioxolan-2-yl)acetate (**15c**)

From **14c** (0.10 g, 0.56 mmol) and Rh_2(*S*-DOSP)$_4$ (21 mg, 0.011 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(4-bromophenyl)acetate (0.28 g, 1.12 mmol) in $PhCF_3$ (5 ml). Yield: 0.13 g (59%), colorless oil; $R_f = 0.42$ (PMA, petroleum ether/diethyl ether 5:1). ee (Chiralcel OD-H 4 × 250 mm, 1% isopropanol in hexanes, 1 ml/min, 230 nm): 75% (major: 18.6 min; minor: 7.8 min). IR (film): $\nu = 2964$ (w), 2893 (w), 1743 (s), 1489 (m), 1149 (s), 1012 (s), 831 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 1.21$ (t, $J = 7.7$ Hz, 3H), 2.61 (q, $J = 7.7$ Hz, 2H), 3.57 (s, 3H), 3.69–3.91 (m, 4H), 4.14 (s, 1H) 7.07 (d, $J = 8.4$ Hz, 2H), 7.19 (d, $J = 8.4$ Hz, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 7.35 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 15.3$ (CH_3), 29.4 (CH_2), 51.8 (CH_3), 59.9 (CH), 64.8, 65.3 (both CH_2), 109.1, 121.8 (both C), 126.1, 127.2, 130.8, 132.0 (all CH), 132.6, 137.7, 144.2, 170.1 (all C). HRMS (ESI): Calc. for $C_{20}H_{21}BrO_4Na$ 427.0515; found 427.0512 – Calc. for $C_{20}H_{21}{}^{81}BrO_4Na$ 429.0495; found 429.0503.

3.9. (S)-Methyl 2-(4-bromophenyl)-2-(2-(-methoxyphenyl)-1,3-dioxolan-2-yl)acetate (**15d**) and methyl 2-(4-bromophenyl)-3-(4-methoxyphenyl)-1,4-dioxane-2-carboxylate (**16**)

From **14d** (0.09 g, 0.49 mmol) and Rh_2(*R*-DOSP)$_4$ (18 mg, 0.01 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(4-bromophenyl)acetate (0.25 g, 0.98 mmol) in $PhCF_3$ (5 ml). **15d**: Yield: 50 mg (25%), colorless oil; $R_f = 0.54$ (PMA, petroleum ether/ethyl acetate 5:1). ee (Chiralcel OD-H 4 × 250 mm, 1% isopropanol in hexanes, 1 ml/min, 230 nm): 74% (major: 18.6 min; minor: 21.4 min); **16**: Yield: 66 mg (33%), colorless oil; $R_f = 0.28$ (PMA, petroleum ether/ethyl acetate 5:1). ee (Chiralcel OD-H 4 × 250 mm, 1% isopropanol in hexanes, 1 ml/min, 230 nm): 47% (major: 21.3 min; minor: 25.9 min). **15d**: IR (film): $\nu = 2950$ (m), 2892 (m), 2838 (m), 1739 (s), 1608 (m), 1508 (m), 1249 (s), 1153 (s), 906 (s), 829 (m), 729 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 3.59$ (s, 3H), 3.71–3.80 (m, 2H), 3.78 (s, 3H), 3.83–3.92 (m, 2H), 4.13 (s, 1H), 6.77 (d, $J = 8.8$ Hz, 2H), 7.21 (d, $J = 8.8$ Hz, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 7.36 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 51.9$, 55.1 (both CH_3), 59.9 (CH), 64.8, 65.2 (CH_2), 109.0 (C), 113.0 (CH), 121.8 (C), 127.5, 130.8, 132.0 (all CH), 132.5, 132.6, 159.4, 170.1 (all C). HRMS (ESI): Calc. for $C_{19}H_{19}O_5BrNa$ 429.0308; found 429.0315 – Calc. for $C_{19}H_{19}O_5{}^{81}BrNa$ 431.0288; found 431.0303. **16**: IR (film): $\nu = 2953$ (w), 2877 (w), 2836 (w), 1735 (s), 1610 (m), 1511 (s), 1247 (s), 1178 (m), 1008 (m), 731 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 3.37$ (dd, $J = 12.3$, 3.3 Hz, 1H), 3.72 (s, 3H), 3.79 (ddd, $J = 12.3$, 12.3, 3.3 Hz, 1H) 3.80 (s, 3H), 4.02 (dd, $J = 12.3$, 3.3 Hz, 1H), 4.26 (ddd, $J = 12.3$, 12.3, 3.3 Hz), 6.71 (d, $J = 8.9$ Hz, 2H), 7.31 (s, 4H), 7.35 (d, $J = 8.9$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 53.1$, 55.0 (CH_3) 57.5, 64.1 (CH_2), 76.2 (CH), 81.4 (C), 113.1 (CH), 121.9, 126.7 (both C), 126.9, 131.3, 132.4 (CH), 137.2, 158.9, 171,8 (all C). HRMS (ESI): Calc. for $C_{19}H_{19}BrO_5$ 406.0410; found 406.0403 – Calc. for $C_{19}H_{19}{}^{81}BrO_5$ 408.0390; found 408.0392.

3.10. (S)-Methyl 2-phenyl-2-(2-styryl-1,3-dioxolan-2-yl)acetate (**18a**)

To a stirred solution of **17** (0.12 g, 0.68 mmol) and Rh_2(*S*-DOSP)$_4$ (26 mg, 0.014 mmol) in $PhCF_3$ (5 ml) at 25 °C was added methyl 2-diazo phenylacetate (0.24 g,

1.36 mmol) in $PhCF_3$ (7 ml) via a syringe pump over 2 h. The reaction mixture was stirred at 25 °C for 1 h and then concentrated in vacuo. The crude product was purified via column chromatography (petroleum ether/diethyl ether 5:1) to afford **18a** (0.12 g, 53%) as colorless oil; $R_f = 0.44$. ee (Chiralcel OD-H 4 × 250 mm, 2% isopropanol in hexanes, 1 ml/min, 254 nm): 84% (major: 18.2 min; minor: 20.8 min). IR (film): $\nu = 3028$ (w), 2951 (w), 2891 (w), 1738 (s), 1448 (w), 1155 (m), 972 (w), 744 (s), 731 (s), 694 (s) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.67$ (s, 3H), 3.84–3.94 (m, 4H), 4.09 (s, 1H), 6.25 (d, $J = 15.7$ Hz, 1H), 6.59 (d, $J = 15.7$ Hz, 1H), 7.21–7.36 (m, 8H), 7.47–7.49 (m, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 51.9$ (CH_3), 59.6 (CH), 64.8, 65.4 (both CH_2), 108.4 (C), 126.8, 127.0, 127.6, 127.9, 128.0, 128.4, 130.0, 131.4 (all CH), 133.6, 136.1, 171.7 (all C). HRMS (ESI): Calc. for $C_{20}H_{20}O_4Na$ 347.1254; found 347.1245.

3.11. (S)-Methyl 2-(4-bromophenyl)-2-(2-styryl-1,3-dioxolan-2-yl)acetate (**18b**)

From **17** (0.10 g, 0.56 mmol) and Rh_2(*S*-DOSP)$_4$ (21 mg, 0.011 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(4-bromophenyl)acetate (0.28 g, 1.10 mmol) in $PhCF_3$ (6 ml). Yield: 0.15 g (65%), colorless oil; $R_f = 0.28$ (petroleum ether/diethyl ether 5:1). ee (Chiralcel OD-H 4 × 250 mm, 2% isopropanol in hexanes, 1 ml/min, 254 nm): 86% (major: 28.6 min; minor: 19.3 min). IR (film): $\nu = 2951$ (w), 2891 (w), 1740 (s), 1489 (m), 1161 (s), 1012 (s), 737 (s), 692 (s) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.68$ (s, 3H), 3.82–3.96 (m, 4H), 4.04 (s, 1H), 6.20 (d, $J = 15.8$ Hz, 1H), 6.59 (d, $J = 15.8$, 1H), 7.25–7.44 (m, 9H). ^{13}C NMR ($CDCl_3$): $\delta = 52.0$ (CH_3), 58.9 (CH), 64.8, 65.4 (both CH_2), 108.2, 122.0 (both C), 126.7, 126.8, 128.1, 128.5, 131.1, 131.7, 131.8 (all CH), 132.7, 135.8, 170.3 (C). HRMS (ESI): Calc. for $C_{20}H_{19}BrO_4Na$ 425.0359; found 425.0370 – Calc. for $C_{20}H_{19}{}^{81}BrO_4Na$ 427.0338; found 427.0340.

3.12. (S)-Methyl 2-(2-styryl-1,3-dioxolan-2-yl)-2-p-tolylacetate (**18c**)

From **17** (0.10 g, 0.56 mmol) and Rh_2(*S*-DOSP)$_4$ (21 mg, 0.011 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(*p*-tolyl)acetate (0.21 g, 1.12 mmol) in $PhCF_3$ (6 ml) added over 4 h via syringe pump. Yield: 0.11 g (57%), colorless oil; $R_f = 0.32$ (petroleum ether/diethyl ether 5:1). ee (Chiralcel OD-H 4 × 250 mm, 2% isopropanol in hexanes, 1 ml/min, 254 nm): 88% (major: 20.0 min; minor: 23.8 min). IR (film): $\nu = 3026$ (w), 2950 (w), 2884 (w), 1740 (s), 1269 (m), 1157 (m), 1040 (m), 970 (m), 754 (s), 739 (s), 692 (s) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 2.32$ (s, 3H), 3.67 (s, 3H), 3.88–3.93 (m, 4H), 4.05 (s, 1H), 6.26 (d, $J = 16.1$ Hz, 1H), 6.60 (d, $J = 16.1$ Hz, 1H), 7.10 (m, 2H), 7.24–7.37 (m, 7H). ^{13}C NMR ($CDCl_3$): $\delta = 21.0$, 51.9 (both CH_3), 59.2 (CH), 64.8, 65.3 (CH_2), 108.5 (C), 126.8, 127.0, 127.9, 128.5, 128.7, 129.8, 130.6, 131.3 (all CH), 136.0, 137.3, 170.8 (all C). HRMS (ESI): Calc. for $C_{21}H_{22}O_4Na$ 361.1410; found 361.1406.

3.13. (S)-Methyl 2-(4-methoxyphenyl)-2-(2-styryl-1,3-dioxolane-2-yl)acetate (**18d**)

From **17** (0.10 g, 0.56 mmol) and Rh_2(*S*-DOSP)$_4$ (21 mg, 0.011 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(4-methoxyphenyl)acetate (0.23 g, 1.12 mmol) in $PhCF_3$ (10 ml). Yield: 0.12 g (62%), colorless oil; $R_f = 0.32$ (petroleum ether/diethyl ether 5:1). ee (Chiralcel AS-H 4 × 250 mm, 0.8% isopropanol in hexanes, 0.5 ml/min, 254 nm): 91% (major: 27.5 min; minor: 32.9 min). IR (film): $\nu = 3025$ (m), 2952 (m), 2893 (m), 1741 (s), 1611 (s), 1513 (s), 1250 (s), 1179 (s), 1037 (s), 834 (s), 759 (m), 744 (m), 694 (m) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.68$, 3.78 (both s, 3H), 3.85–3.96 (m, 4H), 4.04 (s, 1H), 6.25 (d, $J = 16.3$ Hz, 1 h), 6.59 (d, $J = 16.3$ Hz, 1H), 6.83 (d, $J = 8.8$ Hz, 2H), 7.22–7.36 (m, 5H), 7.39 (d, $J = 8.8$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 51.9$, 55.0 (both CH_3), 58.7 (CH), 64.8, 65.3 (CH_2), 108.4 (C), 113.4 (CH), 125.7 (C), 126.8, 127.0, 127.9, 128.5, 131.1, 131.3 (all CH), 136.0, 159.1, 170.9 (all C). HRMS (ESI): Calc. for $C_{21}H_{22}O_5Na$ 377.1359; found 377.1371.

3.14. (S)-Methyl 2-(naphthalen-3-yl)-2-(2-styryl-1,3-dioxolan-2-yl)acetate (**18e**)

From **17** (0.13 g, 0.74 mmol) and Rh_2(*S*-DOSP)$_4$ (28 mg, 0.015 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(2-naphthyl)acetate (0.33 g, 1.48 mmol) in $PhCF_3$ (7 ml). Yield: 0.16 g (59%), white solid m.p. = 118 °C; $R_f = 0.43$ (petroleum ether/diethyl ether 5:1). ee (Chiralcel OD-H 4 × 250 mm, 2% isopropanol in hexanes, 1 ml/min, 254 nm): 73% (major: 24.9 min; minor: 35.5 min). IR (KBr): $\nu = 2950$ (m), 1741 (s), 1599 (w), 1535 (w), 1160 (m), 1044 (m), 834 (m), 752 (m) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.67$ (s, 3H), 3.82–3.95 (m, 4H), 4.27 (s, 1H), 6.29 (d, $J = 15.6$ Hz, 1H), 6.64 (d, $J = 15.6$ Hz, 1H), 7.21–7.34 (m, 5H), 7.42–7.47 (m, 2H), 7.64 (d, $J = 8.7$ Hz, 1H), 7.77–7.84 (m, 3H), 7.94 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 52.03$ (CH_3), 59.7 (CH), 64.8, 65.4 (both CH_2), 108.5 (C), 125.9, 126.8, 127.1, 127.4, 127.9, 128.0, 128.1, 128.5, 129.3 (all CH), 131.1 (C), 131.5 (CH), 132.8, 133.0, 136.0, 170.7 (all C). HRMS (ESI): Calc. for $C_{24}H_{22}O_4Na$ 397.1410; found 397.1407. Anal. Calc. for $C_{24}H_{22}O_4$ (374.43): C, 76.99; H, 5.92. Found: C, 76.60; H, 5.95.

3.15. (S)-Methyl 2-(4-chlorophenyl)-2-(2-styryl-1,3-dioxolan-2-yl)acetate (**18f**)

From **17** (0.20 g, 1.12 mmol) and Rh_2(*R*-DOSP)$_4$ (42 mg, 0.022 mmol) in $PhCF_3$ (5 ml) and methyl 2-diazo-(4-chlorophenyl)acetate (0.48 g, 2.28 mmol) in $PhCF_3$ (10 ml). Yield: 0.21 g (51%), colorless oil; $R_f = 0.5$ (petroleum ether/diethyl ether 5:1). ee (Chiralcel OD-H 4 × 250 mm, 2% isopropanol in hexanes, 1 ml/min,

254 nm): 85% (major: 18.7 min; minor: 29.3 min). IR (film): $\nu = 2950$ (w), 2892 (w), 1739 (s), 1492 (m), 1161 (s), 1091 (m), 806 (m), 744 (m), 694 (m) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.68$ (s, 3H), 3.83–3.95 (m, 4H), 4.06 (s, 1H), 6.21 (d, $J = 16.2$ Hz, 1H), 6.59 (d, $J = 16.2$ Hz, 1H), 7.25–7.35 (m, 7H), 7.42–7.44 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 52.1$ (CH_3), 58.8 (CH), 64.9, 65.4 (both CH_2), 108.3 (C), 126.7 126.8, 128.0, 128.1, 128.5, 131.5, 131.7 (all CH), 132.1, 133.7, 135.8, 170.4 (all C). HRMS (ESI): Calc. for $C_{20}H_{20}ClO_4$ 359.1045; found 359.1042.

3.16. (S)-Methyl 2-(2-(4-methoxystyryl)-1,3-dioxolan-2-yl)-2-(4-bromophenyl)acetate (**18g**) and methyl 3-(4-methoxystyryl)-2-(4-bromophenyl)-1,4-dioxane-2-carboxylate (**20**)

From **19** (0.1 g, 0.48 mmol) and Rh_2(*R*-DOSP)$_4$ (17 mg, 0.009 mmol) $PhCF_3$ (5 ml) and methyl 2-diazo-(4-bromophenyl)acetate (0.24 g, 0.96 mmol) $PhCF_3$ (5 ml). **18g**: Yield: 46 mg (22%), colorless oil; $R_f = 0.50$ (PMA, petroleum ether/diethyl ether 1:1). ee (Chiralcel OD-H 4×250 mm, 3% isopropanol in hexanes, 1 ml/min, 230 nm): 81% (major: 16.8 min; minor: 22.3 min); **20**: Yield: 0.13 g (49%), colorless oil; $R_f = 0.21$ (PMA, petroleum ether/diethyl ether 1:1). ee (Chiralcel OD-H 4×250 mm, 5% isopropanol in hexanes, 1 ml/min, 254 nm): 0% (14.1 min, 14.9 min). **18g**: IR (film): $\nu = 2954$ (w), 2877 (w), 2838 (w), 1735 (s), 1604 (m), 1511 (m), 1245 (s), 1103 (m), 1006 (m), 821 (m), 775 (m), 732 (m) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.70$ (s, 3H), 3.83 (s, 3H), 3.85–3.96 (m, 4H), 4.06 (s, 1H), 6.08 (d, $J = 16.2$ Hz, 1H), 6.56 (d, $J = 16.2$ Hz, 1H), 6.87 (d, $J = 8.8$ Hz, 2H), 7.30 (d), 7.39 (d, $J = 8.3$ Hz 2H), 7.39 (d, 8.8 Hz, 2H), 7.44 (d, $J = 8.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 52.1$, 55.3 (both CH_3), 59.1 (CH), 64.8, 65.4 (both CH_2), 108.4 (C), 114.0, 124.5 (both CH), 127.8 (C), 128.1, 131.1, 131.2, 131.9 (all CH), 132.8, 159.6, 170.4 (all C). **20**: IR (film): $\nu = 2954$ (w), 2931 (w), 2873 (w), 2838 (w), 1735 (s), 1604 (m), 1511 (s), 1245 (s), 1103 (s), 1010 (s), 821 (m), 775 (m), 732 (m) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.50$ (dd, $J = 11.5$, 2.2 Hz, 1H), 3.78 (s, 3H), 3.81 (s, 3H), 3.96 (dd, $J = 11.5$, 2.2 Hz, 1H), 4.05–4.19 (m, 2H), 5.24 (d, $J = 7.7$ Hz, 1H), 6.08 (dd $J = 16.0$, 7.7 Hz), 6.61 (d, $J = 16.0$ Hz, 1H), 6.79 (d, 8.8 Hz, 2H), 7.15 (d, $J =$ 8.8 Hz, 2H), 7.36 (d, $J = 8.8$ Hz, 2H), 7.43 (d, $J = 8.8$ Hz, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 53.0$, 55.2 (both CH_3), 58.6, 63.8 (both CH_2), 76.3 (CH), 81.5 (C), 113.8, 120.4 (both CH), 122.3 (C), 126.9, 127.7 (both CH), 129.0, 131.2 (both C), 131.5, 136.4 (both CH). HRMS (ESI): Calc. for $C_{21}H_{21}BrO_5$ 432.0567; found 432.0555 – Calc. for $C_{21}H_{21}{}^{81}BrO_5$ 434.0546; found 434.0539.

3.17. (S)-Methyl 2-(4-bromophenyl)-2-(2-(2-phenylethynyl)-1,3-dioxolan-2-yl)acetate (**24**)

To a stirred solution of **23** (0.1 g, 0.57 mmol) and Rh_2(*S*-DOSP)$_4$ (21 mg, 0.011 mmol) in $PhCF_3$ (5 ml) at 25 °C was added methyl 2-diazo-(4-bromophenyl)acetate (0.29 g, 1.14 mmol) in $PhCF_3$ (5 ml) via a syringe pump over 2 h. The reaction mixture was stirred at 25 °C for 1 h and then concentrated in vacuo. The crude product was purified via column chromatography (petroleum ether/diethyl ether 5:1) to afford **24** (0.16 g, 68%) as colorless oil; $R_f = 0.50$. ee (Chiralcel OD-H 4×250 mm, 2% isopropanol in hexanes, 1 ml/min, 254 nm): 86% (major: 20.1 min; minor: 25.6 min). IR (film): $\nu = 2950$ (w), 2896 (w), 2225 (w), 1739 (s), 1488 (m), 1157 (s), 756 (s), 732 (s), 690 (s) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.74$ (s, 3H), 3.93–3.99 (m, 2H), 4.12–4.17 (m, 2H), 4.21 (s, 1H), 7.26–7.39 (m, 5H), 7.48 (pseudo-s, 4H). ^{13}C NMR ($CDCl_3$): $\delta = 52.3$ (CH_3), 59.1 (CH), 65.3, 65.4 (both CH_2), 85.0, 86.0, 102.6, 121.6, 122.5 (all C), 128.2, 128.9, 131.2, 131.8, 131.9, 132.1 (all CH), 132.1, 169.9 (both C). HRMS (ESI): Calc. for $C_{20}H_{17}BrO_4Na$ 423.0202; found 423.0199 – Calc. for $C_{20}H_{17}{}^{81}BrO_4Na$ 425.0182; found 425.0187.

3.18. (S,E)-Methyl 4-phenyl-2-(2-phenyl-1,3-dioxolan-2-yl)but-3-enoate (**26**)

To a stirred solution of **9** (0.1 g, 0.69 mmol) and Rh_2(*S*-DOSP)$_4$ (104 mg, 0.055 mmol) in 2,2-DMB (10 ml) at 25 °C was added (*E*)-methyl 2-diazo-4-phenylbut-3-enoate (0.28 g, 1.38 mmol) in 2,2-DMB (10 ml) via a syringe pump over 2 h. The reaction mixture was stirred at 25 °C for 1 h and then concentrated in vacuo. The crude product was purified via column chromatography (petroleum ether/diethyl ether 5:1) to afford **26** (0.10 g, 46%) as colorless oil; $R_f = 0.25$. ee (Chiralcel AS-H 4×250 mm, 0.5% isopropanol in hexanes, 0.8 ml/min, 254 nm): 89% (major: 15.5 min; minor: 19.4 min). IR (film): $\nu = 2951$ (w), 2918 (w), 2850 (w), 1732 (s), 1431 (w), 1236 (m), 1028 (m), 991 (m), 754 (s), 696 (s) cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 3.52$ (s, 3H), 3.67 (d, $J = 8.2$ Hz, 1H), 3.71–3.73 (m, 2H), 3.96–3.99 (m, 2H), 6.21–6.29 (m, 2H), 7.11–7.25 (m, 8H), 7.37 (m, 2H). ^{13}C NMR ($CDCl_3$): $\delta = 51.9$ (CH_3), 59.4 (CH), 64.9, 65.2 (both CH_2), 109.4 (C), 122.5 (CH), 126.2,.126.4, 127.6, 127.8, 128.3, 128.4, 134.8 (all CH), 136.6, 140.4, 170.5 (all C). HRMS (ESI): Calc. for $C_{20}H_{20}O_4Na$ 347.1254; found 347.1246. Anal. Calc. for $C_{20}H_{20}O_4$ (324.37): C, 74.06; H, 6.21. Found: C, 73.96; H, 6.31.

3.19. (R)-3-Hydroxy-1,2-diphenylpropan-1-one (**27**)

From **12a** 0.14 g (0.52 mmol) and iodine (13 mg, 0.05 mmol) in acetone (20 ml) analogously to published procedure [48]. Yield: 78 mg (66%), slightly yellow oil; $R_f = 0.3$ (petroleum ether/diethyl ether 1:4). Identity of **26** confirmed by comparison with published data [49].

3.20. (1S,2R)-1,2-Diphenylpropane-1,3-diol (**28**)

From **27** (30 mg, 0.13 mmol), NaH (4 mg, 0.17 mmol) $TiCl_4$ (0.17 ml, 1 M in CH_2Cl_2) and $LiBH_4$ (4 mg,

0.18 mmol) in THF (5 ml) as published [49]. Identity of **28** confirmed by comparison with published data [49].

3.21. Competition study: formation of (*S*)-methyl 2-phenyl-2-(2-styryl-1,3-dioxolan-2-yl)acetate (*18a*) vs. (2*R*,3*S*)-methyl 3-(tert-butyldimethylsiloxy)-2,5-diphenylpent-4-enoate (*22*)

The setup of the reaction follows the general procedure established in our laboratory to asses reactivity differences of substrates in C–H insertion reactions [27].

To a stirred solution of **17** (0.35 g, 2.0 mmol), **21** (0.49 g, 2.0 mmol) and Rh_2(*S*-DOSP)$_4$ (8 mg, 0.004 mmol) in $PhCF_3$ (10 ml) at 25 °C was added methyl 2-diazo-phenylacetate (88 mg, 0.5 mmol) in $PhCF_3$ (2.5 ml) via a syringe pump over 2 h. The reaction mixture was stirred at 25 °C for 1 h, concentrated in vacuo and excess substrate was removed via Kugelrohr distillation. ^{1}H NMR and ESI-MS analysis of the residual green oil revealed that **22** [27] was the only product formed in the reaction.

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