

A Modular Olefination of Aldehydes with Thiols as Coupling Partners

Sabine Bogner^[a] and Manuel van Gemmeren^{*[a, b]}

Dedicated to Prof. Dr. Ulrich Lüning on the occasion of his retirement

Abstract: Olefins range amongst the most important motifs in organic chemistry. Hence, the development of novel olefin syntheses has remained a constant field of research in synthetic chemistry to date. Herein, we report the development of a modular olefination that converts aldehydes into olefins with thiols as reaction partners. The simple, transition metal-free protocol proceeds via an unsymmetrical bisulfone intermediate which is converted into the respective alkene in

a Ramberg-Bäcklund-type process. Differently substituted olefins can be synthesized from readily available starting materials in typically good yields and stereoselectivities using basic laboratory chemicals exclusively. Complementary reaction conditions differing in the choice of solvent favor the *E*/*Z*-products respectively under kinetic control rendering this protocol an interesting economical addition to the family of olefin syntheses.

Introduction

Olefins are a key functional motif in organic chemistry, that occur in important natural products, drugs, polymers, and functional materials and are highly versatile synthetic intermediates.^[1] The central importance of the olefin moiety for synthetic chemistry is reflected in the vast number of procedures that have been developed for their synthesis, three of which have been awarded with a Nobel prize,^[2] and the ongoing interest to improve and add to the tools available in this field.^[3] There are two main approaches for the synthesis of olefins: the synthesis from an already existing alkene (or alkyne) and the *de novo* formation of the C=C bond. While the first group includes mainly transition metal-catalyzed transformations like olefin metathesis,^[4] cross-couplings,^[5] and hydrogenations,^[6] the second group spans from simple eliminations to the olefination of aldehydes,^[7] arguably the most important method for *de novo* synthesis of olefins. In such olefinations, the C=C bond is generated from an aldehyde (or carbonyl) and a specific reaction partner designed to induce the

desired process (Scheme 1a). Famous examples of such reagents include phosphorous ylids (Wittig),^[8] phosphonates (Horner-Wadsworth-Emmons),^[9] phenyl sulfones (Julia),^[10] heteroaromatic sulfones (Julia-Kocienski),^[11] silanes (Peterson),^[12] or titanium alkylidenes (Tebbe).^[13] Recently, Maulide and co-workers added sulfoxonium and thiuronium ylides to the range of reaction partners in carbonyl olefination.^[14] This report, in which olefins are formed through a cheletropic cycloreversion, demonstrates the continued interest in the development of novel olefination processes. Importantly, the availability of various methods for the synthesis of olefins is essential, as these methods complement one another, for example with respect to the reaction conditions used, the substitution patterns/stereoselectivities that can be achieved, and the availability of the respective coupling partners. When studying different olefination protocols, we noticed that the substrates of the traditional Ramberg-Bäcklund rearrangement (RBR),^[15,16] α -chloro-sulfones **3**, bear a carbon atom on the aldehyde oxidation level as it is found in commonly used olefination protocols of aldehydes (Scheme 1a and b).

We thus wondered whether it would be possible to condense an aldehyde, a thiol and a potential leaving group, oxidize the sulfur center and subsequently effect an RBR-type step to obtain a novel olefination method starting from readily available aldehydes (**1**) and thiols (**2**, Scheme 1b). Interestingly, there is currently no method using thiols, an important class of organic compounds, as coupling partner in the olefination of aldehydes. Notably, our strategy also differs drastically from traditional synthetic sequences involving Ramberg-Bäcklund rearrangements, which typically involve several nucleophilic substitutions, as well as oxidation and α -chlorination steps.^[16,17] Moreover, our idea would involve a cheletropic cycloreversion as olefin-forming step which, to the best of our knowledge, has only been reported once for an aldehyde olefination^[14a] involving completely different reagents.

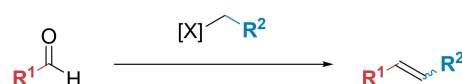
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a. Traditional Approach: Olefination of Aldehydes



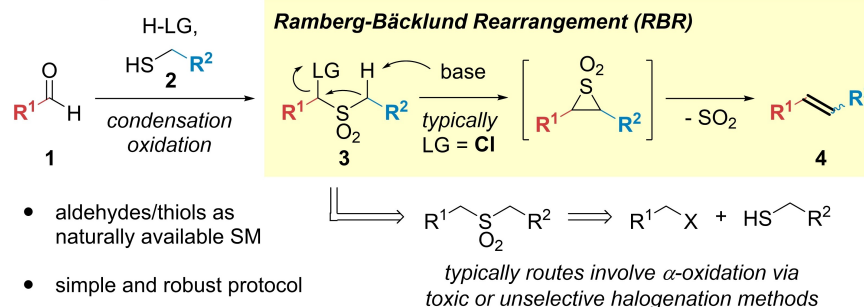
⇒ Complementary regarding:

- *E/Z*-selectivity
- substituent/ FG tolerance
- reagent availability

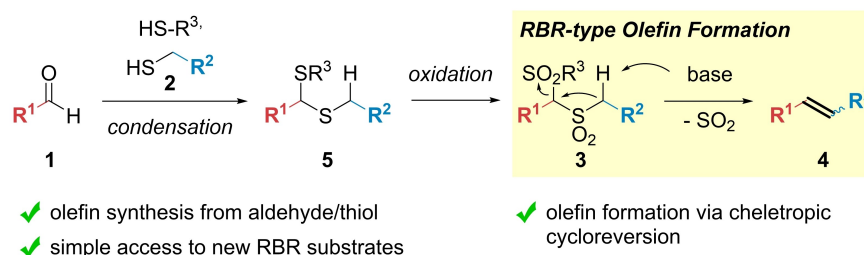
Various Named Reactions

$[\text{X}] = \text{Ph}_3\text{P}^+\text{CH}_2\text{R}^2$	Wittig
$(\text{RO})_2\text{P}(\text{O})\text{CH}_2\text{EWG}$	HWE
$\text{R}_3\text{SiCH}_2\text{R}^2$	Peterson
$\text{Ar}^{\text{Het}}\text{O}_2\text{SCH}_2\text{R}^2$	Julia
...	...

b. Our Design



c. This Work



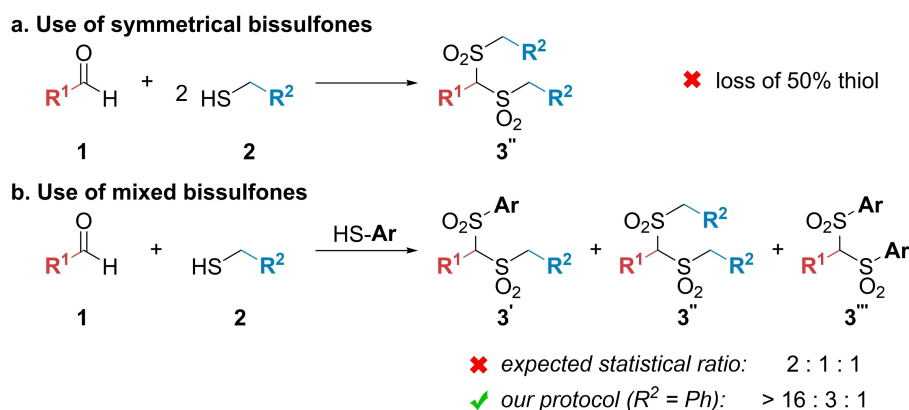
Scheme 1. Overview of a) traditional aldehyde olefinations, b) our design and c) process developed in this study.

After considerable experimentation we found that the envisioned sequence can be achieved using sulfonates as leaving group via dithioacetal (5) and bissulfone intermediates (3, Scheme 1c). The use of sulfonate rather than chloride leaving group in RBRs has received little attention in the literature, presumably due to the challenging substrate syntheses and low yields reported by the few reports available.^[17,18]

In our case, the use of symmetrical dithioacetals 5'' and bissulfones (3'') would require an excess of the thiol component 2, a key drawback for the potential use of valuable thiol reaction partners (Scheme 2a). We hypothesized that a protocol using equimolar amounts of both reaction partners might be enabled by the formation of mixed dithioacetals (5') and bissulfones (3'), in which the role of each thiol, either as part of the product or the leaving group, would be defined by using one aromatic and one aliphatic thiol. However, no general method for the selective formation of such mixed compounds existed at the outset of our studies, prompting us to develop a

kinetically controlled protocol for the selective formation of mixed dithioacetals (Scheme 2b), which can then be converted to the respective bissulfones.^[19]

Overall, our approach relies on the formation of a mixed dithioacetal 5', its oxidation to an unsymmetric bissulfone 3', and a Ramberg-Bäcklund-type olefin formation. Importantly, due to the kinetically controlled dithioacetal formation a strong selectivity for the mixed bissulfone (3') is observed. All steps developed are robust and use conditions known to generally work well in the context of complex molecule synthesis, leading us to the expectation that a broadly applicable overall process might result. Ideally, we envisaged that several of these steps might be combined into one operation. Herein, we report the development of such a protocol for the synthesis of differently substituted olefins from carbonyls and thiols with a Ramberg-Bäcklund-type olefination step.



Scheme 2. Strategic approach towards the use of equimolar amounts of the thiol reaction partner.

Results and Discussion

We began our studies by investigating different sulfinate leaving groups choosing benzaldehyde **1a** and benzyl mercaptan **2a** as model substrates to give unsubstituted stilbene **4a** as the final product. 4-chlorothiophenol was found to give the best results as leaving group component both in terms of reactivity and cost. All three steps of the protocol (thioacetalization, oxidation, olefin formation) were then optimized separately (see the Supporting Information for details on the optimization studies). An adapted version of our previous protocol^[15] delivered mixed *S,S*-acetals under kinetic control (alongside minor quantities of the symmetric analogues). These could be oxidized to the corresponding bissulfones using standard oxidation reagents urea hydrogen peroxide complex^[20] or *m*CPBA without changing the ratio between the components. Interestingly, the thus obtained unsymmetrical *gem*-bissulfones (**3'**) represent an almost unexplored class of organic compounds that turned out to be stable under ambient conditions for more than two years.

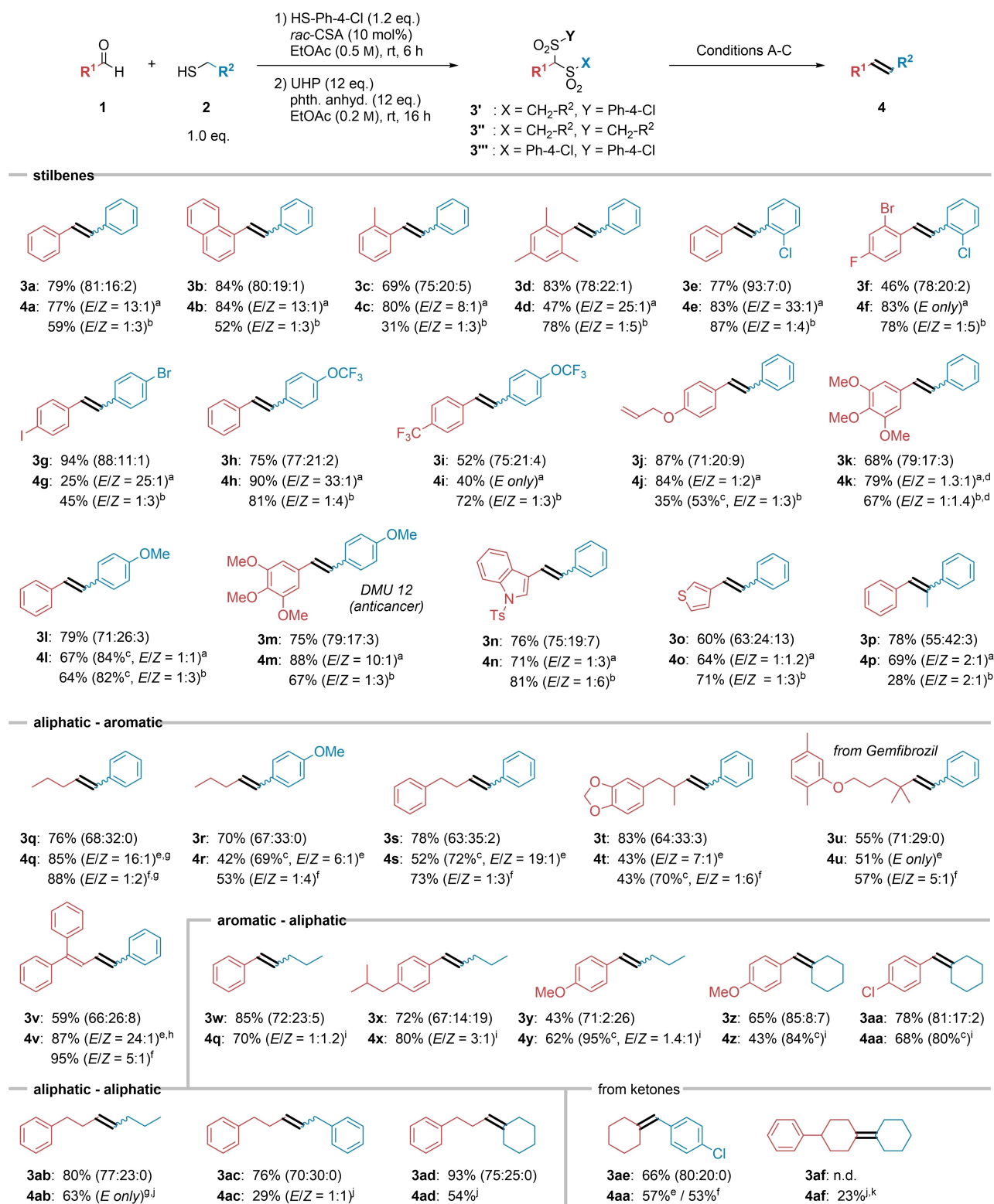
Importantly, it was not necessary to separate the mixed bissulfone from the two symmetrical by-products since two of the three components, **3'** and **3''** (generally amounting to 95% of the mixture) can further react to the olefin product. The third component (**3'''**), which generally accounts for less than 5% of the mixture, remains inert during the olefin formation after which it can easily be separated from the olefin product. Finally, the first two steps of acetalization and oxidation were combined into one operational procedure without any intermediate purification.

After screening different bases and solvents as well as optimizing all other reaction parameters, we found three sets of conditions for the olefin-forming step depending on the type of olefin to be formed (see Supporting Information for details). Notably, for bissulfones derived from benzylic thiols, a switch of solvent led to a switch in *E/Z*-selectivity in the target olefin.

With the optimized conditions in hand, we began to investigate the scope of this protocol (Scheme 3). For all entries, the yield of the bissulfone mixture intermediate **3** and the olefin product **4** are given to illustrate the compatibility of different

substrates with both steps of the protocol. First, different stilbene derivatives were synthesized using LiOtBu as a base and *t*AmylOH or DCE as a solvent (Conditions A). Unsubstituted stilbene **4a** and 2-naphthaldehyde-derived stilbene **4b** were obtained in high yields and excellent *E*-selectivity in *t*AmylOH as solvent, while a switch to the solvent DCE delivered majorly the *Z*-product. Notably, the traditional Ramberg-Bäcklund rearrangement with chloride leaving groups has been reported to be *E*-selective in such processes.^[15b] Stilbene **4c** synthesized from mono *ortho*-substituted benzaldehyde **1c** was isolated with the same selectivity in respect to the solvent used and similar trends in yield. However, two *ortho*-substituents on the aldehyde starting material led to a decrease in yield to 47% under the *E*-favoring conditions (**4d**) while the same starting material delivered the *Z*-olefin in 78% yield and a 1:5-ratio when reacted in DCE. Products **4e** and **4f** with a bulky *ortho*-substituent on the thiol reagent were each obtained in high yields and good selectivities under both sets of reaction conditions.

Notably, olefins like **4f** and **4g**, with multiple different halogen substituents, are challenging to obtain via standard methods involving transition metals or organolithium reagents. Particularly iodine and bromine substituents (**4g**) are valuable for further functionalization. Electron-withdrawing substituents were also tolerated on both reaction partners (**4h**, **4i**). In particular, when the electron-withdrawing substituent was located only on the former thiol part, an excellent conversion and *E*-selectivity were observed (**4h**). Product structures containing electron-rich substituents were also compatible with the protocol giving olefins **4j–4m** in 64%–88% yield but in some cases deviated from the previously observed *E/Z*-selectivity. An allyl ether substituent in para-position of the benzaldehyde substrate (**4j**) switched the selectivity in *t*AmylOH towards the *Z*-configured stilbene. In DCE, the selectivity remained in favor of the *Z*-olefin as observed before, but the reaction slowed substantially, with significant amounts of unreacted starting material being reisolated after the standard reaction time. 3,4,5-Trimethoxy benzaldehyde derived stilbene **4k** was obtained in good yields in both solvents but with modest stereoselectivity in both cases. However, despite the reduced selectivity *E-4k*



Scheme 3. Scope of the olefination protocol. The first line of results indicates yields and ratios (3':3'':3''') of the isolated bissulfone mixtures 3 synthesized on a 1.0 mmol scale. The second (and third) line shows yield and selectivity of the olefination step conducted on a 0.2 mmol scale. For entries showing several reaction conditions, the same batch of starting material was used. For simplicity, the final olefin products are shown while the bissulfones are depicted in the Supporting Information. a) Conditions A1: LiOtBu (1.5 equiv.), *t*AmylOH (0.05 M), 120 °C, 24 h. b) Conditions A2: LiOtBu (1.5 equiv.), DCE (0.05 M), 120 °C, 24 h. c) Yield based on recovered starting material. d) The *E*- and *Z*-isomer were separated on column and obtained in pure form. For simplicity, the combined result is given. e) Conditions B1: NaOH (3.0 equiv.), *t*AmylOH (0.05 M), 120 °C, 24 h. f) Conditions B2: NaOH (3.0 equiv.), DCE (0.05 M), 120 °C, 24 h. g) Yield determined via GC-FID analysis with 1,3,5-trimethoxybenzene (TMB) as internal standard. h) Reaction performed under Argon atmosphere. i) Conditions C: NaOH (3.0 equiv.), toluene (0.05 M), 140 °C, 24 h. j) Conditions C with 72 h reaction time. k) Reaction performed on a 1 mmol scale.

and **Z-4k** were isolated isomerically pure after separation by column chromatography. When an electron-donating substituent was situated on the thiol component (**4l**) the olefin was formed in 64%–67% yield. Electron-rich substituents on both reaction partners yielded anticancer agent DMU-212^[21] (**4m**) with good yields and selectivities under both sets of reaction conditions. This entry underlines the potential of our protocol for an economic and operationally simple alternative to access valuable olefins. Even heteroaromatics such as indoles (**4n**) and thiophenes (**4o**) were tolerated under the developed conditions. Finally, trisubstituted olefin **4p** was synthesized in 69% yield in *t*AmylOH with the *E*-isomer as the main product. The same selectivity was also observed in DCE where only 28% of olefin were isolated, presumably because the product structure itself strongly favors the *E*-configuration.

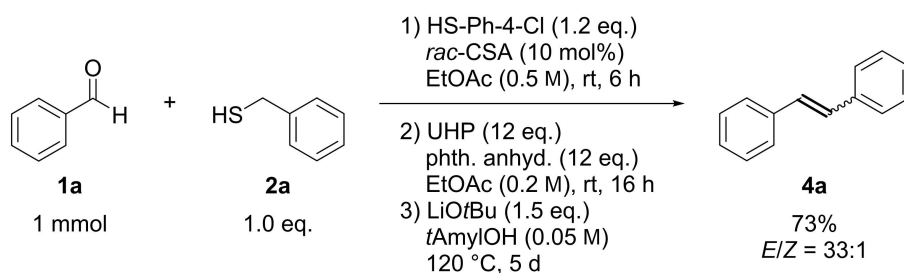
Next, we investigated the combination of aliphatic aldehydes with benzylic thiols. We again observed that a change in solvent from *t*AmylOH to DCE shifted the preferred stereochemistry of the target olefin from *E* to *Z*, but best results were obtained when NaOH was used as base (Conditions B). Olefins **4q–4s**, derived from aliphatic aldehydes, were obtained in good yields and similar *E/Z*-selectivities as before. The natural fragrance helional was also tolerated by our protocol delivering olefin **4t** with standard selectivity. While a secondary carbon in α -position to the aldehyde (**4t**) did not affect the configuration of the formed double bond, a tertiary carbon in this position favored the formation of the *E*-isomer in both solvents, for example in the case of the drug derivative **4u**. An exception of the expected selectivity was observed for product **4v**, that formed the *E*-isomer preferentially in both solvents in excellent yields likely due to the conjugated system being formed. Interestingly, the same product structures, with one aliphatic and one aromatic substituent on the double bond, can be formed when using a benzaldehyde starting material with an aliphatic thiol. Olefin **4q** could indeed be synthesized from both permutations of starting materials (**3q** and **3w**), but for **3w** a third set of olefination conditions with NaOH as base, toluene as solvent and an elevated reaction temperature was required (Conditions C). Under this set of conditions, olefins **4q**, **4x**, and **4y** were synthesized in good yields but with reduced stereoselectivity. The lower in *E/Z*-selectivity as well as the reduced reaction rate observed for some of these examples are likely linked to the properties of the α -methylene-position, the deprotonation of which will lead to product formation. In case of bissulfone substrates **3q** to **3v** that originate from an

aliphatic aldehyde and a benzylic thiol, deprotonation in the α -position is stabilized by the neighboring arene. In contrast, bissulfones obtained from an aromatic aldehyde and an aliphatic thiol, lack this stabilizing effect in the deprotonation step. This stabilization is also absent in a fourth class of products: olefins with two aliphatic substituents. Gratifyingly, aliphatic aldehydes and aliphatic thiols could nevertheless be combined in our protocol using elevated temperature and extended reaction times (Conditions C), giving access to products **4ab–4ad**. Interestingly, Olefin **4ab** was obtained as pure *E*-isomer which represents a selectivity contrary to the standard Wittig protocol for such products.

Additionally, the compatibility of ketones with our protocol was investigated. Olefin **4aa** could not only be synthesized from 4-chlorobenzaldehyde and cyclohexane thiol (intermediate **3aa**) in 68% yield but also from cyclohexanone and 4-chlorobenzyl mercaptan (intermediate **3ae**) using Conditions B. Interestingly, our method even allowed for the synthesis of tetrasubstituted olefin **4af** in 23% yield using Conditions C. In this case, the yield and ratio of the intermediate bissulfones were not determined due to the complexity of the respective NMR spectrum, but the complete protocol was carried out from ketone and thiol to olefin without any intermediate characterization. Overall, even though the selectivities obtained are in some cases moderate, they generally compare well to those of standard olefination methods. Various products from stilbenes to olefins with only aliphatic substituents could be synthesized, a range otherwise only covered by Wittig and Julia olefinations, both of which require several synthetic steps to access the respective reagents, while thiols are a broad and often commercially available substrate class.

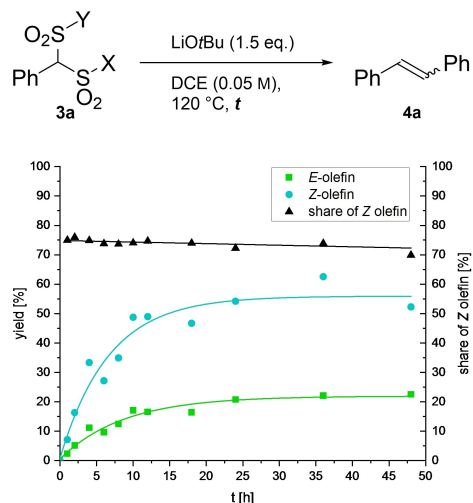
To demonstrate the synthetic utility of our protocol we performed the reaction of benzaldehyde with benzyl mercaptan in *t*AmylOH on a 1 mmol scale without an intermediate characterization (Scheme 4). Stilbene **4a** was obtained in overall 73% yield and very high *E*-selectivity. This result underlines the utility of our protocol to generate olefins in synthetically useful overall yields starting from aldehydes and thiols in an operationally simple overall process. Furthermore, the entire process involved only one aqueous workup on the way from aldehyde to isolation of the final olefin.

In order to obtain more information on the solvent-dependent switch in *E/Z*-selectivity we conducted isomerization experiments using standard product stilbene **4a**. During the optimization studies, we had observed that in *t*AmylOH the *E*-isomer

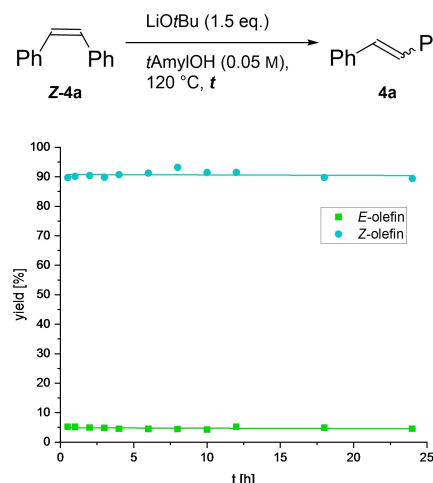


Scheme 4. Application of the full protocol on a 1 mmol scale.

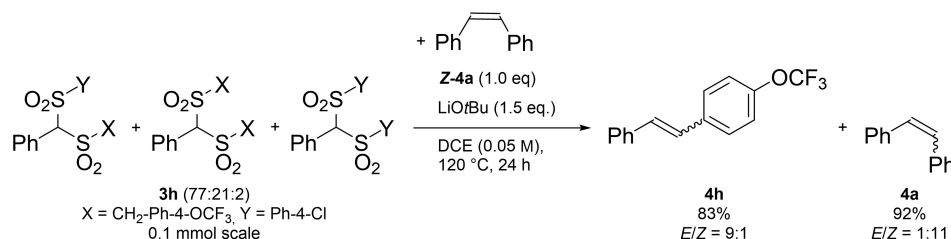
a. Z-product formation over time



b. Isomerization under E-conditions



c. Isomerization under full experimental conditions



Scheme 5. Mechanistic studies: a) product formation over time under Z-conditions, b) configurational stability of Z-stilbene under E-conditions, c) and configurational stability of Z-stilbene as additive during the synthesis of E-olefin. All experiments were performed on a 0.1 mmol scale. For experiments (a) and (b), yields were determined by GC-FID analysis using 1,3,5-trimethoxybenzene as internal standard. For experiment (c), yields and ratios were determined by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard.

forms preferentially from the beginning of the reaction (see Scheme S10). Analogously, the formation of **4a** in DCE was monitored over time (Scheme 5a). Z-stilbene **4a** was formed as the major product from the beginning, with the ratio of Z to E staying constant over the course of the reaction, indicating that no thermal isomerization occurs under these reaction conditions.

We next probed, if such an isomerization can occur in *t*AmylOH by exposing the pure Z-olefin to the E-favoring conditions (Scheme 5b). In this experiment no significant isomerization to the E-olefin was observed. Furthermore, isomerically pure Z-**4a** was added to the synthesis of **4h** in *t*AmylOH (Scheme 5c). Again, no significant isomerization of Z-**4a** was detected, while the formation of **4h** was unaffected by the additional olefin present. The experiments from Scheme 5(b and c) allow us to exclude a scenario where the Z-olefin forms as the kinetic product under the E-favoring conditions, but is then transformed into the E-isomer in a fast equilibration leading to thermodynamic control. We can thus conclude that the E/Z-selectivity of our protocol is kinetically controlled for both stereoisomers. The polarity of the solvent seems to influence the transition state or intermediate that defines the stereochemical outcome of the reaction, an observation that agrees well with studies on the selectivity of related Ramberg-

Bäcklund rearrangements and the Julia-Kocienski olefination.^[11,22]

Conclusion

In summary, we have developed an olefination of aldehydes with thiols as coupling partners, which complements the existing portfolio of carbonyl olefination methods. Mixed bissulfones are generated through an operationally simple combination of dithioacetal formation and oxidation, which are then converted into an olefin in a Ramberg-Bäcklund-type cheletropic cycloreversion. Notably, our study constitutes the first synthetically useful example of sulfinat leaving groups in Ramberg-Bäcklund-type processes and the first general access to unsymmetrical *gem*-bissulfones, a previously almost unexplored compound class. Three sets of olefination conditions differing in terms of base and solvent enable the synthesis of diversely substituted aromatic and aliphatic alkenes including examples that are challenging to obtain via standard olefination methods. For several important product classes, the E/Z-selectivity can be switched under kinetic control based on the choice of solvent. The modular nature of our protocol and the use of simple, readily available, standard reagents render our

method an attractive addition to the tools available for olefin synthesis that can be applied by a wide range of synthetic chemists. We are confident that this work sets the foundation for further studies on the use of thiols as coupling partners in aldehyde olefination.

Experimental Section

General Procedure for the synthesis of bissulfones with urea·H₂O₂ as oxidant: In an oven-dried Schlenk tube (10 mL), 4-chlorobenzenethiol (0.17 g, 1.2 mmol, 1.2 equiv.) and *rac*-camphor-10-sulfonic acid (23 mg, 0.1 mmol, 0.1 equiv.) were dissolved in EtOAc (0.5 M, 2 mL). The respective thiol (1.0 mmol, 1.0 equiv.) and the respective aldehyde (1.0 mmol) were added. The resulting reaction mixture was stirred at room temperature for 6 h (750 rpm stirring speed). The crude *S,S*-acetal mixture was filtered over a short plug of Na₂SO₄ (3 cm in a glass pipette) washing with EtOAc (3×1 mL). Urea hydrogen peroxide (0.65 g, 12 mmol, 12 equiv.) and phthalic anhydride (1.8 g, 12 mmol, 12 equiv.) were added to the resulting filtrate and this mixture was stirred vigorously over night at room temperature. The resulting suspension was diluted with EtOAc (10 mL) and H₂O (15 mL) and the phases were separated. The organic layer was washed with aqueous NaOH solution (1 M, 4×10 mL), H₂O (15 mL), and brine (15 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The obtained bissulfone mixture was dried under vacuum before further use.

General Procedure for the synthesis of bissulfones with mCPBA as oxidant: In an oven-dried 10 mL Schlenk tube, 4-chlorobenzenethiol (0.17 g, 1.2 mmol, 1.2 equiv.) and *rac*-camphor-10-sulfonic acid (23 mg, 0.1 mmol, 0.1 equiv.) were dissolved in EtOAc (0.5 M, 2 mL) before the respective thiol (1.0 mmol, 1.0 equiv.) and the respective aldehyde (1.0 mmol) were added. The resulting reaction mixture was stirred at room temperature for 6 h (750 rpm stirring speed). The crude *S,S*-acetal mixture was filtered over a short plug of Na₂SO₄ (3 cm in a glass pipette) washing with EtOAc (3×1 mL) and concentrated. The residue was dissolved in CH₂Cl₂ (5 mL) and *m*CPBA (1.8 g, 8.0 mmol, 8.0 equiv.) was added portion wise (4 portions, every hour) at room temperature. After the second and the third addition the resulting slurry was diluted with more CH₂Cl₂ (2×3 mL). The resulting mixture was stirred vigorously over night at room temperature and then diluted with CH₂Cl₂ (10 mL) and H₂O (10 mL). The phases were separated, and the organic layer was washed with aq. sat. NaHCO₃ solution (2×10 mL) and aq. sat. Na₂SO₃ solution (2×10 mL) to remove remaining peroxide. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The obtained bissulfone mixture was dried under vacuum before further use.

General procedure for the olefination using conditions A: An oven-dried Schlenk tube (10 mL) was charged with the corresponding bissulfone mixture (0.2 mmol, 1.0 equiv.) and LiOtBu (24 mg, 0.3 mmol, 1.5 equiv.). The respective solvent (4 mL, *t*AmylOH or DCE) was added and the reaction mixture was stirred in a pre-heated metal block at 120 °C for 24 h (stirring speed 1000 rpm). After cooling down to room temperature the crude product mixture was diluted with H₂O (2 mL) and EtOAc (2 mL). The phases were separated, and the organic phase was washed with brine (10 mL), dried over Na₂SO₄, filtered, and concentrated. The respective target compound was obtained after purification by flash column chromatography. Note Conditions A1 (*E*-olefin favoured): solvent = *t*AmylOH; Conditions A2 (*Z*-olefin favoured): solvent = DCE

General procedure for the olefination using conditions B: An oven-dried Schlenk tube (10 mL) was charged with the corresponding bissulfone mixture (0.2 mmol, 1.0 equiv.) and NaOH (24 mg,

0.6 mmol, 3.0 equiv.). The respective solvent (4 mL, *t*AmylOH or DCE) was added and the reaction mixture was stirred in a pre-heated metal block at 120 °C for 24 h (stirring speed 1000 rpm). After cooling down to room temperature the crude product mixture was diluted with H₂O (2 mL) and EtOAc (2 mL). The phases were separated, and the organic phase was washed with brine (10 mL), dried over Na₂SO₄, filtered, and concentrated. The respective target compound was obtained after purification by flash column chromatography. Note: Conditions B1 (*E*-olefin favoured): solvent = *t*AmylOH; Conditions B2 (*Z*-olefin favoured): solvent = DCE.

General procedure for the olefination using conditions C: An oven-dried Schlenk tube (10 mL) was charged with the corresponding bissulfone mixture (0.2 mmol, 1.0 equiv.) and NaOH (24 mg, 0.6 mmol, 3.0 equiv.). Toluene (4 mL) was added. The reaction mixture was stirred in a pre-heated metal block at 140 °C for 24 h or 72 h (stirring speed 1000 rpm). After cooling down to room temperature the crude product mixture was diluted with H₂O (2 mL) and EtOAc (2 mL). The phases were separated, and the organic phase was washed with brine (10 mL), dried over Na₂SO₄, filtered, and concentrated. The respective target compound was obtained after purification by flash column chromatography.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: aldehydes · kinetic control · olefination · Ramberg-Bäcklund · rearrangement · thiols

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