Tetrahedron 68 (2012) 10378-10390

Contents lists available at SciVerse ScienceDirect

Tetrahedron

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

Alkoxyl radical addition to acceptor-substituted carbon-carbon double bonds

Irina Kempter, Andreas Groß, Jens Hartung*

Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, D-67663 Kaiserslautern, Germany

ARTICLE INFO

Article history: Received 22 June 2012 Received in revised form 24 August 2012 Accepted 27 August 2012 Available online 1 September 2012

Keywords: Acrylate Acrylonitrile Addition Alkoxyl radical Amino acid Bromo-cyclization Borderline reactivity Radicals Stereoselective synthesis Thiazolethione

ABSTRACT

Alkoxyl radicals add 5-*exo-trig* selectively to cyano- and methoxycarbonyl-substituted carbon–carbon double bonds, to afford α -acceptor- α -tetrahydrofuryl-2-methyl radicals. Trapping of cyclized radicals by Bu₃SnD furnishes products of site-specific deuterium-labeling in α -position to the acceptor group. In intramolecular competition experiments, alkoxyl radicals add similarly fast to a cyano-substituted double bond than to a terminal alkene, but by a factor >25 faster to an enol ether. The nucleophilic component of alkoxyl radical reactivity opens an interesting new access to tetrahydrofuryl amino acids via C,O-cyclization, as shown by synthesis of a *N*,*O*-protected 5-phenyltetrahydrofuryl-2-methyl glycine. © 2012 Elsevier Ltd. All rights reserved.

1. Introduction

The oxygen nucleus attracts an unpaired valence electron in alkoxyl radicals stronger than the carbon nucleus in alkyl radicals. Oxygen radicals therefore attack higher in energy σ - and π -bonds with a reactivity/selectivity profile that is characteristic for many electrophiles.^{1,2} Since oxygen forms strong bonds to hydrogen and carbon, the odd electron in alkoxyl radicals gives rise to chemical reactivity that is by orders of magnitude higher than carbon radical reactivity. Typical examples for reactions that take profit from unique alkoxyl radical reactivity are found in metabolic pathways,³ and in oxidative hydrocarbon degradation, which clear the atmosphere from volatile organic compounds.^{4,5}

In spite of enormous reactivity, alkoxyl radicals generally react selectively, following guidelines that allow to apply the intermediates in organic synthesis.¹ A method that has received growing attention for stereoselective synthesis within the past decade is the alkoxyl radical addition to carbon–carbon double bonds.^{6–8} The current mechanistic picture shows that alkoxyl radicals add to constitutionally dissymmetric π -bonds with selectivity that often complements additions of alcohols or alkoxides to

oxidatively activated alkenes. Additions of oxygen radicals that are too slow to compete with other radical consuming processes, such as β -fragmentation^{9–11} or homolytic substitution,¹² generally are accelerated by substituting the carbon double bond with typical donor groups, such as methyl, phenyl, or silyloxy.^{13–16} A drawback for pursuing new reactions in alkoxyl radical chemistry in synthesis, however, is the inherent electrophilicity, restricting selectivity control by the polar effect so far exclusively to donor substituents.

The scope of alkoxyl radical chemistry extends, if the intermediates add to Michael-type acceptors. In a communication on alkenoxyl radical generation from O-phenylsulfenates for studying stereochemical aspects of 4-pentenoxyl radical cyclization,¹⁷ αmethacrylate-type double bonds were used as O-radical acceptors, however, without addressing the role of the polar effect.¹⁸ In view of the potential arising from a nucleophilic component in alkoxyl radical reactivity, we decided to explore in a systematic manner addition to acrylate- and acrylonitrile-type π -bonds, lacking in an activating α -methyl group (Fig. 1). The major results from the study show that 4-pentenoxyl radicals add to the cyano-substituted carbon-carbon double in a rate that compares to the rate of addition to a terminal double bond. The fastest reaction in the series of competition experiments, however, is addition to an enol ether π -bond. From this dichotomic behavior we concluded that alkoxyl radicals are both, electrophiles and nucleophiles, depending on substitution at the π -bond. We used the nucleophilic component of





^{*} Corresponding author. Tel.: +49 631 205 2431; fax: +49 631 205 3921; e-mail address: hartung@chemie.uni-kl.de (J. Hartung).

^{0040-4020/\$ –} see front matter @ 2012 Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.tet.2012.08.083



Fig. 1. Structure, substituent effects, and proposed chemical reactivity of alkoxyl radicals used in this study to explore the polar effect in additions to carbon–carbon double bonds.

alkoxyl radical reactivity to develop a new route to synthesis of a *N*,*O*-protected tetrahydrofuryl-2-methyl amino acid via C,Ocyclization.

2. Results and interpretation

2.1. Alkoxyl radical generation and synthesis of radical precursors

We applied O-alkenyl thiohydroxamates of the type 1 in this study as alkoxyl radical progenitors. The compounds add electrophilic radicals Y• at the thione sulfur, which causes the nitrogen-oxygen bond to homolytically break. Radicals used for inducing alkoxyl radical liberation from 1 generally originate from an initiator, such as α,α -azobisisobutyronitrile (AIBN), or from a mediator X-Y in a propagating step of a chain reaction (Scheme 1). Typical mediators X–Y used in this chemistry are tributylstannane, the deuterium derivative Bu₃SnD for isotope labeling, and bromotrichloromethane. An alternative approach to oxygen radical generation from **1** is photochemistry. Excitation of electronic transitions in the molecule, by shining light into the broad electronic band at ~335 nm, selectively induces homolysis of the nitrogen-oxygen bond. The reaction between chain propagating radical Y• and O-alkenyl thiohydroxamate 1 thus provides alkenoxyl radical 2 and substituted thiazole **3**.^{5,19} For synthesis of tetrahydrofurans (e.g. **5**), bimolecular trapping of alkenoxyl radical 2 by the mediator X-Y must be slower than the cyclization $2 \rightarrow 4$.^{20–23} Trapping of carbon radical 4 by the mediator provides target product 5 and supplies the chain with propagating radical Y•.5



Scheme 1. Steps for alkoxyl radical generation in a chain reaction between *N*-alkoxy-thiazole-2(3*H*)-thione **1** (R=e.g. CH₃ or Ph; A=e.g. CN, CO₂CH₃; An=*p*-anisyl, i.e. *p*-methoxyphenyl) and a mediator X–Y (Bu₃SnH, Bu₃SnD, or BrCCl₃).

For synthesis of alkenyl thiohydroxamates **1a**–**i**, cyclic thiohydroxamic acid 6 was esterified by alkenols using the Mitsunobumethod, or a procedure that we refer to as the salt-method (Scheme 2, Supplementary data, and Experimental). Selectivity in the salt-method follows Pearson's principle of hard soft acids and bases. O-Alkylation at the hard oxygen instead of soft sulfur is attainable with a hard carbon electrophile, reacting with a thiohydroxamate anion experiencing no contact from a hard, strongly polarizing cation. This approach is put into practice by converting acid 6 into tetraethylammonium salt 7, which subsequently is treated in a strongly polar aprotic solvent, such as dimethyl formamide, with an alkenyl chloride (for **1a–e**) or a tosylate (for **1i**) (Table 1). In the Mitsunobu-method, the electrophile is generated in situ from an alkenol and the combination of diethyl azodicarboxylate (DEAD) and triphenylphosphine in a solution of benzene, to furnish O-alkenyl thiohydroxamates **1f**-**h** and **1j** in yields between 31 and 67% (Fig. 2). After chromatographic purification, the target compounds were received as colorless (1g-i) to yellow (1a-e, 1j) compounds, which are stable for months if stored in a refrigerator. O-Alkenyl thiohydroxamates of the type 1 show characteristic electronic spectra having a broad band located at $\lambda = 332 - 338 \text{ nm} (\lg \epsilon \sim 3.00 - 3.28 \text{ m}^2 \text{ mol}^{-1}, \text{ in EtOH for } 1a - c, \text{ and}$ CHCl₃ for 1d), which allows to photoexcite the molecules for homolytically breaking the nitrogen-oxygen bond (vide supra).





Scheme 2. Methods for synthesis of alkoxyl radical precursors of the type **1** [for yields, see Table 1 and Fig. 2; X=Cl, OTs; R=alkenyl; all reactions were performed at 20-25 °C].

Table 1

Yields of ester- and cyano-substituted *N*-alkenoxythiazolethiones **1a**–**e** prepared from alkenyl chlorides via the salt-method^a



1а-е

Entry	1	\mathbb{R}^1	R ²	А	Yield/%	(E)/(Z)
1	а	CH ₃	Н	CN	36	77:23
2	b	C_6H_5	Н	CN	49	76:24
3	с	CH ₃	Н	CO ₂ CH ₃	49	>98:2
4	d	C_6H_5	Н	CO ₂ CH ₃	70	>98:2
5	e	C ₆ H ₅	cyclo-C ₃ H ₅	CN	73	62:38

^a (RX=RCl, cf. Scheme 2; MAnTT=5-(4-methoxyphenyl)-4-methyl-2-thiooxo-2,3-dihydrothiazol-3-yl).

	\searrow	OM	Ph (S) CO ₂ Et NHAc		
1	\mathbb{R}^1	\mathbb{R}^2	yield / %	(E): (Z)	(S)- 1j (31%)
f	CH ₃	CH ₃	60	_	(E):(Z) > 98:2
g	Η	OCH ₃	67	80:20	
h	Η	CN	63	72:28	
i	Η	CO ₂ Et	49	>98:2	

Fig. 2. Structure formulas, indexing of compounds, and yields of N-alkenoxythiazolethiones 1f-j (Mitsunobu-method for 1f-h and 1j, and salt-method for 1i from the alkenyl tosylate).

2.2. Alkoxyl radical addition to acceptor-substituted carbon–carbon double bonds

In the standard approach to tetrahydrofuran synthesis we photolyzed cyano-substituted alkenoxythiazolethiones 1a-b and ester derivatives 1c-d with near UV-light (350 nm) in solutions of benzene containing 3.7 equiv of tributylstannane (c^0 =185 mM). From the solutions, we isolated 2,5-disubstituted tetrahydrofurans **5a**–**d**, as mixtures of cis/trans-stereoisomers in yields between 67 and 71% (Table 2, entries 1–2 and 4–5). The trans-stereoisomer of heterocycles **5a**–**d**, in all instances, is the major product, as derived from stereochemical analysis by proton NMR, carbon-13 NMR, and NOESY-spectroscopy. For supplementing the mass balance and supporting the mechanistic interpretation, we quantified in all instances tributylstannylsulfanylthiazole **3a**. This compound forms in 99% to quantitative yield, but decomposes upon contact with silica gel used for separating tetrahydrofurans **5a–d**, particularly from residual organotin compounds. Since we had fully characterized stannylated thiazole **3a** in a previous study, we restricted ourselves at this point to identifying heterocycle 3a by proton NMR-spectroscopy.⁵ A supplementary photoreaction performed with Bu₃SnD as mediator, provides tetrahydrofuran $5b_{d1}$ in 74%, bearing the deuterium label exclusively in α -position to the cyano group (Table 2, entry 3).

possibly from β -carbon—carbon fragmentation of alkoxyl radicals or *O*-alkenyl thiohydroxamates **1a**–**d**. Authentic references of the assumed products were available from the synthetic part of the study. None of the assumed products, however, had formed in sufficient amounts for being detected, under conditions applied to prepare **5a**–**d**.

In controls to investigate whether tetrahydrofuran **5b** possibly had formed from an alkoxide-mediated cyclization, we treated 1phenyl-6-hydroxyhex-2-enenitrile, the underlying alcohol of **1b**, with tributylstannane in benzene. Also, we stirred 50/50-mixtures of this alcohol and the derived ketone in a solution containing tributylstannane for 90 min in the dark, and in a photoreactor shining 350 nm-light into the sample. From the controls, we exclusively recovered the starting materials. The only chemical change we noticed was a photoisomerization at the double bond of 6-phenyl-6-hydroxyhex-2-enenitrile from (E)/(Z)=87:13 to 51:49.

From a boiling solution of *O*-alkenyl thiohydroxamate **1d** in benzene, containing 0.5 M concentration of bromotrichloromethane and minor amounts of azobisisobutyronitrile (AIBN) to initiate the reaction, we isolated 62% of α -thiazylsulfanyl ester **8d** in a cis/transratio of 43:57, 21% of α -bromoester **9d** as 44/56-mixture of cis/transisomers, and 30% of trichloromethylsulfanylthiazole **3b** (Scheme 3). From this result we concluded that regio- and stereoselectivity of intramolecular carbon–oxygen bond formation are independent

Table 2

Products of reductive 3-alkenoxythiazole-2(3H)-thione (MAnTTOR) conversion



Entry	1/5	R	А	Х	5 /% (<i>cis/trans</i>) ^a	3a /% ^b
1	a ^b	CH ₃	CN	Н	69 (38:62)	99
2	b	C ₆ H ₅	CN	Н	67 (44:56)	quant.
3	bc	C ₆ H ₅	CN	D	74 (46:54)	d
4	c	CH3	CO ₂ CH ₃	Н	68 (37:63)	99
5	ď	C ₆ H ₅	CO ₂ CH ₃	Н	71 (41:59)	quant.

^a Relative tetrahydrofuran configuration at C2 and C5; 50/50-ratio of stereoisomers with respect to C_{α} .

^b From reaction mixtures via ¹H NMR-spectroscopy (pentachlorobenzene as internal standard).

^c Compound indexing for **5**: **b**_{d1}.

^d Not determined.

In routine analysis of product mixtures obtained from reactions between tributylstannane and O-alkenyl thiohydroxamates **1a**–**d**, we searched via GC–MS and NMR-spectroscopy for additional products that could have been formed, for example, alcohols from alkoxyl radical reduction by tributylstannane, aldehydes or ketones from the chemical nature of the mediator, as predicted on the basis of the general mechanistic scheme for *O*-alkenyoxythiazolethione conversion under conditions that favor homolytic reactions (Scheme 1). The preference for thioether- over alkyl bromide formation in this experiment arises from the low affinity of the



Scheme 3. Selectivity of product formation from ester-substituted thiazolethione 1d and BrCCl₃ (R=CH₃). ^a Relative configuration at C2 and C5; 50/50-ratio of stereoisomers at C_a.

intermediate electrophilic α -alkoxycarbonyl alkyl radical, for abstracting a bromine atom from bromotrichloromethane.^{24–26}

From a photolyzed solution of benzene containing bromotrichloromethane and 2-cycano-2-cyclopropyl-substituted thiazolethione **1e**, we isolated 64% of α -substituted pentenonitrile **5** ϵ , 16% of ketone **10**, and 41% of trichloromethylsulfanylthiazole **3b** (Scheme 4). The appearance of ketone **10** in this experiment surprised us, although ketone formation from secondary benzylic *N*-alkenoxythiazolethiones is not an entirely new reaction. Benzylic *N*-alkenoxythiazolethiones tend to dissociate into a thiolactam and a carbonyl compound in a nonradical reaction, if stored, heated, or photolyzed.²⁷ a β-fragmentation pathway, to furnish, in extension to arguments provided in the previous paragraph, a carbon radical that is trapped by bromotrichloromethane. The mechanism that combines adequate reactivity with selectivity to explain formation of (δ-bromo-α-cyanobutenyl)tetrahydrofuran **5**ε under such conditions is the cyclopropylmethyl to butenyl radical ring opening,²⁹ which in turn points to an alkoxyl radical addition mechanism to the cyano-substituted double bond in **2**ε.

(iii) Stereoselectivity for tetrahydrofuran formation from 1a-e leaves a fingerprint-type 60/40-selectivity in favor of the 2,5-



Scheme 4. Formation of α -(phenyltetrahydrofuryl)- δ -bromopentenonitrile 5 ϵ from 2-cyclopropyl-2-cyano-substituted thiazolethione 1e [62:38-mixture of (*E*)/(*Z*)-isomers].^a (*E*)/(*Z*)-isomers].^a (*E*)/(*Z*)-isomers].^a (*E*)/(*Z*)-isomers].^b Relative tetrahydrofuran configuration at C2 and C5.

Regarding the general mechanism, we think for the following four reasons that synthesis of side chain acceptor-substituted tetrahydrofurans from *N*-alkenoxythiazolethiones 1a-e having Michael-type carbon–carbon double bonds, follows the general alkoxyl radical pathway (Scheme 1):

- (i) The concluding step of the tetrahydrofuran synthesis is hydrogen atom transfer from Bu₃SnH to a reactive intermediate, deuterium-labeling by Bu₃SnD, or bromination by BrCCl₃. The three reagents have in common to favor homolytic substitution by carbon radicals to reactions with cations or anions.²⁸ The position of site specific labeling, deuteration for synthesis of tetrahydrofuran **5b**_{d1} and bromination for synthesis of α-bromoester **9d**, correlates with the proposed position of a carbon radical in the intermediate (Schemes 1 and 5).
- (ii) The fact that α -cyano- α -cyclopropyl-substituted *N*-alkenoxythiazolethione **1e** furnishes exclusively (δ -bromo- α -cyanobutenyl)tetrahydrofuran **5** ϵ , and not (α -bromo- α cyclopropyltetrahydrofuryl)acetonitrile **5e**, shows that the underlying intermediate is able to induce rapid cyclopropyl ring opening (Scheme 5). From the site of bromine labeling, we also knew that the ring opening occurs in

trans-stereoisomer. This value is close to the 65/35-cis/transselectivity for 5-*exo-trig*-cyclization of the (*E*)-1-phenyl-4penten-1-yl radical.³⁰ Alkoxide-based cyclization of 6hydroxy-6-phenyl-2-pentenenitrile, catalyzed by potassium *tert*-butoxide in a solution of ethanol, furnishes a mixture of stereoisomers for tetrahydrofuran **5b**, which is by 52/48 slightly in favor for the cis-isomer.

(iv) The yields of thiazole- and alkoxyl radical-derived products 3 and 5 are in many experiments similar, as predicted from an underlying chain mechanism. In instances of diverging mass balances, we find explanations from the literature that are consistent with homolytic reactions starting from 1a-d. For example, 2-trichloromethylsulfanyl thiazole 3b is a photolabile compound, which gradually decomposes as substrate conversion in a photochemical experiment progresses, thus explaining the low yield of this product.⁵ In other instances (cf. Scheme 4), additional thiazole-derived products appeared. We had described the existence of such products in a previous study dealing with alkoxyl radical generation from tert-O-alkyl thiohydroxamates. Since the new thiazole derivatives now and then remained unidentified we could not use this information for improving the thiazole mass balance.⁷



Scheme 5. Mechanistic interpretation of (cyanobutenyl)tetrahydrofuran formation from cyano-substituted cyclopropylmethyl radical 2e ([Br] symbolizes a homolytically transferable bromine atom, for example, from BrCCl₃).

2.3. Reactivity in intramolecular additions

The affinity for alkoxyl radicals to add to Michael-type carbon– carbon double caused us to address the question on alkoxyl radical polarity in additions by a competition kinetic study. In our approach, we used *N*-dienoxythiazolethiones 1f-i for determining the polar effect of substituents on relative rates in cyclizations.

In the general experimental set-up, solutions of *O*-alkylthiohydroxamates **1f**–**i** ($c^0_{1f-i}=55$ mM) containing tributylstannane ($c^0=205$ mM; Table 3, entries 1–3) or Bu₃SnD (Table 3, entries 4–5) were photolyzed with 350 nm-light until the starting material is entirely consumed.³¹ Methoxy- and dimethyl-substituted thiazolethiones **1f**–**g** provided exclusively products **5f** and **5g** from addition to the donor-substituted double bond (GC, NMR). Acceptor-substituted thiazolethiones **1h**–**i** furnished 52/48- (for R¹=CN, R²=H) and 42/58-mixtures (for R¹=CO₂CH₃, R²=H) of products **5** versus **11** (GC, NMR; 3 independent runs). All cyclizations afforded the *trans*-tetrahydrofuran as major stereoisomer (Table 3).

Alkoxyl radical 5-*exo*-trig cyclization to terminal- and donorsubstituted double bonds, unlike the oxygen radical β -fragmentation,^{32,33} proceed irreversibly,³⁴ and terminal substitution by a polar substituent is not expected to change this situation.³⁵ In this mechanistic interpretation, the ratio of products **5** and **11** directly reflects relative reactivity of the two double bonds for accepting the alkoxyl radical. For the discussion on relative reactivity by comparing results from competition experiments performed under identical conditions, we propose to use the term *relative rate factor* instead of relative rate constant. A relative rate constant is the result of a reaction series performed by parameter variation, providing from numeric analysis the desired kinetic information.

Relative rate factors for alkoxyl radical 5-*exo*-cyclization increase along the series of alkene-substituents R from OCH₃ (from **1g**) and methyl (from **1f**) via H (from **1h** and **1i**) and CN (from **1h**) to CO_2CH_3 (from **1i**; Scheme 6). The fastest (R=OCH₃) and the slowest (R=CO₂CH₃) reaction differ by an approximated factor of 35. This value considers a rate factor of 25 for addition to the enol ether

Table 3

Effect of terminal substituents on regioselectivity in 5-exo-trig alkenoxyl radical cyclization



^a Bu₃SnH for X=H, Bu₃SnD for X=D.

^b cis/trans-Ratios determined via GC, stereochemical assignment via NOESY.

^c Not detected (¹H NMR).

^d (*E*)/(*Z*)=80:20.

e(E)/(Z)=72:28.

 $^{f}(E)/(Z)=46:54.$

^g Compound indexing for 5 and 11: h_{d1}.

^h (*E*)/(*Z*)=53:47.

 $^{i}(E)/(Z) > 98:2.$



Scheme 6. Summary of substituent effects on relative rate factors in alkenoxyl radical cyclization (the open circle symbolizes a phenyl, methyl or a 3-buten-1-yl group).

group in **1g**, based on selectivity for formation of **5g** of larger than 96/4, according results from proton NMR-spectroscopy. From previous work we knew that one methyl group increases the rate of 5-*exo*-trig alkenoxyl radical cyclization by a factor of 5–7, and two methyl groups by a factor of 12–15.^{30,36} We therefore assigned the methoxy group a larger activating effect than the methyl group (Scheme 6).

A gradual increase in relative rate factor in going from substituents R=H via CH₃ to OCH₃ points to an electrophilic behavior of the radical oxygen.³⁷ The progression of the rate factor as R changes from methoxycarbonyl via hydrogen to cyano points to an accelerating contribution of the cyano group, although the effect is small. Since the cyano is the strongest acceptor in the series of investigated substituents, known to activate a conjugated carbon–carbon double bond for addition of nucleophiles to the β -carbon in a reaction known as Micheal-addition, we attribute the driving force of alkoxyl addition to acrylonitrile-type double bonds to nucleophilic behavior of the O-radical.

The underlying theory to explain reactivity and selectivity in alkoxyl radical additions is frontier molecular orbital theory, because the reactions are fast and exothermic and therefore proceed via transition states located early on a reaction coordinate.^{6,38} According to FMO-theory, the major bonding contribution, as the radical approaches the π -bond of the alkene, arises from interactions between the singly occupied molecular orbital (SOMO) and either the highest occupied molecular orbital (HOMO) or the lowest unoccupied molecular orbital (LUMO). As the alkene is substituted by donor groups, such as methoxy or methyl, orbital energies rise and the HOMO-SOMO-interaction becomes more prominent (Fig. 3, right; D=OCH₃, CH₃).^{6,38} Acceptor groups, such as a cyano- or an ester-group, lower orbital energies of the alkene, causing attractive LUMO-SOMO interactions to become more significant (Fig. 3, left; A=CN, CO₂CH₃). Electrophilic radicals (e.g. \cdot CCl₃) have low and nucleophilic radicals [e.g. \cdot C(CH₃)₃] high SOMO-energies. Radicals that interact by their SOMO to a similar extent with the LUMO and the HOMO of an alkene are on the borderline between nucleophilic and electrophilic. The responsivity of substituent effects on rates in alkoxyl radical



Fig. 3. FMO-correlation diagram for explaining borderline reactivity of alkoxyl radicals in additions to substituted alkenes, on the basis of stabilizing interactions in transition states (A=CN, CO₂CH₃; D=CH₃, OCH₃).

additions shows this typical dichotomic behavior of borderline cases, being an electrophile if the alkene bears a donor group, or a nucleophile if the attacked π -bond is substituted by a cyano- or an ester-group (Fig. 3).^{39–41}

2.4. Application in synthesis

The propensity of alkoxyl radicals for adding to acceptorsubstituted double bonds opens new perspectives for synthesis, since substrates now become accessible for homolytic carbonoxygen bond formation that so far were not attainable by this approach. Tetrahydrofurylamino acids have not yet been prepared via C,O-cyclization. Some tetrahydrofuryl amino acids, such as the furanomycin derivatives, show antibiotic activity.⁴² We therefore considered synthesis of a *N*,O-protected tetrahydrofuryl glycine an attractive target for documenting the scope of our findings.

We put our strategy into practice by photolyzing *N*-alkenoxythiazolethione (*S*)-**1j** and tributylstannane in a solution of benzene at room temperature. From the reaction mixture, we isolated *N*,O-protected α -(5-phenyltetrahydrofuran-2-yl)methyl glycine **5j** in a yield of 73%, thus proofing the proposed concept (Scheme 7).



Scheme 7. Synthesis of *N*,*O*-protected 2-(5-phenyltetrahydrofuran-2-yl)methyl glycine **5j** from *N*-alkenoxythiazolethione (*S*)-**1j** and Bu₃SnH (50/50-mixtures of isomers at C_{α}).

3. Concluding remarks

The affinity for adding to cyano- and ester-substituted double bonds in rates that compare to reactivity of terminal alkenes, adds a new component to synthesis with oxygen radicals. From the kinetic information provided in this work it seems that further accepting groups, for example halogens, nitro, or arylsulfonyl, will sufficiently activate alkenes to construct carbon—oxygen bonds via an alkoxyl radical mechanism. The argument, to consider in future syntheses radical and not ionic reactions for addition of oxygen compounds to Michael-type acceptors, possibly arises from stereoselectivity of the ring closure, and diversity of methods available for functionalizing carbon radicals. Alkoxide-based additions to Michael-type acceptors have the disadvantage of being reversible and often difficult to terminate with other reagents than the proton.

Nucleophilic properties of alkoxyl radicals could have been predicted from the day, additions were explained by frontier molecular orbital (FMO)-theory, based on kinetic³⁶ and theoretical data.⁶ In FMO-theory nucleophilicity of an alkoxyl radical is a logical consequence of the LUMO-energy of an accepting entity, for example a π^* -type orbital predominantly located at an alkene subunit, falling below the SOMO energy of the unpaired electron.

We have not yet performed experiments to explore whether borderline reactivity extends to other alkoxyl radical elementary reactions, such as homolytic substitution, rearrangements, or β -fragmentation. Bond formation and bond breaking in all such processes is explicable by FMO-theory. According to FMO-theory, orbital energies of reactants are controlled by substituents in a systematic and predictable manner. We therefore expect borderline reactivity to be a general phenomenon in alkoxyl radical chemistry. Since alkoxyl radicals play an important role in combustion processes, atmospheric chemistry, biochemistry, and synthesis, we think that the findings summarized in this article have the potential to double the scope of alkoxyl radical chemistry.

4. Experimental

4.1. General

For general laboratory practice and instrumentation see Ref. 7 and the Supplementary data.

4.2. 3-Alkoxythiazole-2(3*H*)-thiones 1a-e from alkenyl chlorides

4.2.1. General procedure. An alkenol was dissolved in CCl₄ and treated with PPh₃. The reaction mixture was stirred at 80 °C for 2–4 h. The precipitate was filtered off by suction and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (SiO₂) to afford an alkenyl chloride, which was added to a solution of 3-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt⁴³ in dry DMF. The resulting mixture was stirred at 22 °C for 6–13 days in the dark. The solution was treated at 22 °C with Et₂O or CH₂Cl₂ and H₂O. The aqueous layer was extracted with Et₂O or CH₂Cl₂ and the combined layers were dried (MgSO₄). The solvent was removed under reduced pressure to leave a crude product, which was purified by chromatography (SiO₂).

4.2.2. 3-(1'-Cvanohex-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4methylthiazole-2(3H)-thione (1a). 6-Chlorohept-2-enenitrile: According to 4.2.1 from 6-hydroxyhept-2-enenitrile (1.06 g, 8.47 mmol), PPh₃ (2.89 g, 11.01 mmol) and CCl₄ (10 mL). Reaction time: 3 h. Eluent used for chromatography: pentane/Et₂O=1:1 (v/v). Yield: 879 mg [6.12 mmol, 72%, (*E*)/(*Z*)=83:17], yellow oil, *R*_f 0.63 [SiO₂, pentane/ $Et_2O=1:1 (v/v)$]. (E)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.53 (d, 3H, J 6.4, 7-H), 1.78-1.89 (m, 2H, CH₂), 2.35-2.41 (m, 1H, CH₂), 2.45-2.51 (m, 1H, CH₂), 3.96-4.05 (m, 1H, 6-H), 5.37-5.41 (m, 1H, 2-H), 6.70 (dt, 1H, J_d 16.2, J_t 7.0, 3-H). ¹³C NMR (CDCl₃, 150 MHz) δ 25.3 (C7), 30.4 (CH₂), 37.8 (CH₂), 57.2 (C6), 100.8 (C2), 117.2 (CN), 154.1 (C3). (Z)isomer: ¹H NMR (CDCl₃, 600 MHz) δ 2.53 (d, 3H, J 6.4, 7-H), 1.78–1.89 (m, 2H, CH₂), 2.55-2.67 (m, 2H, CH₂), 3.96-4.05 (m, 1H, 6-H), 5.37–5.41 (m, 1H, 2-H), 6.49 (dt, 1H, J_d 10.9, J_t 7.6, 3-H). ¹³C NMR (CDCl₃, 150 MHz) & 25.2 (C7), 29.1 (CH₂), 38.4 (CH₂), 57.2 (C6), 100.5 (C2), 115.7 (CN), 153.3 (C3). 3-(1'-Cyanohex-1'-en-5'-oxy)-5-(pmethoxyphenyl)-4-methylthiazole-2(3H)-thione (1a): According to 4.2.1 from 6-chlorohept-2-enenitrile (879 mg, 6.12 mmol), 3hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt (2.34 g, 6.12 mmol) and DMF (12 mL). Reaction time: 13 days. The reaction mixture was treated with Et₂O (50 mL) and H₂O (50 mL). The layers were separated and the organic layer was kept. The aqueous layer was extracted with CH₂Cl₂ $(3 \times 50 \text{ mL})$. Eluent used for chromatography: pentane/Et₂O=1:2 (v/v). Yield: 798 mg [2.21 mmol, 36%, (E)/(Z)=77:23], yellow oil, R_f 0.30 [SiO₂, pentane/Et₂O=1:2 (v/v)]. UV (MeOH) λ_{max} $(\lg \epsilon/m^2 \text{ mol}^{-1})=335 \text{ nm}$ (3.25). (E)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.31 (d, 3H, J 6.2, 6'-H), 1.79–1.84 (m, 1H, CH₂), 1.86–1.96 (m, 1H, CH₂), 2.28 (s, 3H, 4-CH₃), 2.58–2.62 (m, 2H, CH₂), 3.83 (s, 3H, OCH₃), 5.42–5.45 (m, 1H, 1'-H), 5.46–5.52 (m, 1H, 5'-H), 6.79–6.84 (m, 1H, 2'-H), 6.95 (d, 2H, J 8.8, Ar–H), 7.24 (d, 2H, J 8.5, Ar–H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.7 (4-CH₃), 18.7 (C6'), 29.2 (CH₂), 33.2 (CH₂), 55.4 (OCH₃), 80.2 (C5'), 100.5 (C1'), 114.5 (Ar-C), 117.4 (CN), 119.5 (C5), 122.5 (Ar-C), 129.8 (Ar-C), 133.2 (C4), 154.8 (C2'), 159.9 (Ar–C), 179.1 (C2). (Z)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.34 (d, 3H, J 6.5, 6'-H), 1.86-1.96 (m, 1H, CH₂), 1.98-2.04 (m, 1H, CH₂), 2.29 (s, 3H, 4-CH₃), 2.66–2.77 (m, 2H, CH₂), 3.83 (s, 3H, OCH₃), 5.37 (d, 1H, J 10.9, 1'-H), 5.46–5.52 (m, 1H, 5'-H), 6.70–6.74 (m, 1H, 2'-H), 6.95 (d, 2H, J 8.8, Ar–H), 7.24 (d, 2H, J 8.5, Ar–H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.7 (4-CH₃), 18.4 (C6'), 27.6 (CH₂), 33.3 (CH₂), 55.4 (OCH₃), 80.3 (C5'), 100.1 (C1'), 114.5 (Ar–C), 115.9 (CN), 119.5 (C5), 122.5 (Ar–C), 129.8 (Ar–C), 133.3 (C4), 154.2 (C2'), 159.9 (Ar–C), 179.1 (C2).

4.2.3. 3-(1'-Cyano-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1b). 6-Chloro-6-phenylhex-2-enenitrile: According to 4.2.1 from 6-hydroxy-6-phenylhex-2enenitrile (1.00 g, 5.34 mmol), PPh₃ (1.82 g, 6.94 mmol) and CCl₄ (6 mL). Reaction time: 4 h. Eluent used for chromatography: pentane/ Et₂O=2:1 (v/v). Yield: 896 mg [4.36 mmol, 82%, (E)/(Z)=88:12], colorless oil, $R_f 0.52$ [SiO₂, pentane/Et₂O=2:1 (v/v)]. (E)-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 2.10–2.48 (m, 4H, CH₂), 4.80–4.84 (m, 1H, 6-H), 5.36 (d, 1H, J 16.2, 2-H), 6.68 (dt, 1H, J_d 16.2, J_t 6.8, 3-H), 7.31–7.37 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 30.7 (CH₂), 37.6 (CH₂), 62.2 (C6), 101.0 (C2), 117.1 (CN), 126.8, 128.6, 128.8, 140.7 (Ph-C), 153.6 (C3). (*Z*)-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 2.10–2.48 (m, 4H, CH₂), 4.80-4.84 (m, 1H, 6-H), 5.42 (d, 1H, J 16.5, 2-H), 6.82 (dt, 1H, Jd 16.2, Jt 6.4, 3-H), 7.31–7.37 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 30.7 (CH₂), 36.0 (CH₂), 62.2 (C6), 100.7 (C2), 117.3 (CN), 126.8, 128.6, 128.8, 140.7 (Ph-C), 153.3 (C3). 3-(1'-Cyano-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1b): According to 4.2.1 from 6-chloro-6-phenylhex-2-enenitrile (519 mg, 2.52 mmol), 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt (1.20 g, 3.14 mmol) and DMF (6 mL). Reaction time: 10 days. The reaction mixture was treated with Et₂O (15 mL) and H₂O (20 mL). The layers were separated and the organic laver was kept. The aqueous laver was extracted with Et₂O $(4 \times 50 \text{ mL})$. Eluent used for chromatography: pentane/Et₂O=1:1 (v/v). Yield: 519 mg [1.23 mmol, 49%, (E)/(Z)=76:24], pale yellow solid, R_f 0.26 [SiO₂, pentane/Et₂O=1:1 (v/v)]. UV (MeOH) λ_{max} $(\lg \epsilon/m^2 mol^{-1})=336 mm (3.28)$. Anal. calcd. for $C_{23}H_{22}N_2O_2S_2$ (422.56): C, 65.38; H, 5.25; N, 6.93; S, 15.17; found: C, 65.27; H, 5.12; N, 6.69; S, 15.04. (*E*)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.50 (s, 3H, 4-CH₃), 2.15–2.20 (m, 1H, CH₂), 2.54–2.70 (m, 3H, CH₂), 3.79 (s, 3H, OCH₃), 5.44 (d, 1H, J 16.4, 1'-H), 6.19 (t, 1H, J 6.7, 5'-H), 6.79-6.84 (m, 1H, 2'-H), 6.86 (d, 2H, 18.7, Ar-H), 6.99 (d, 2H, 18.7, Ar-H), 7.35-7.45 (m, 5H, Ph-H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.1 (4-CH₃), 29.8 (CH₂), 30.4 (CH₂), 55.4 (OCH₃), 84.9 (C5'), 100.7 (C1'), 114.4 (Ar-C), 117.4 (CN), 118.5 (C5), 122.5 (Ar-C), 128.9, 129.0, 129.8, 130.2 (Ph-C and Ar-C), 133.7 (C4), 136.2 (Ph-C), 154.5 (C2'), 159.8 (Ar-C), 178.5 (C2). (Z)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.52 (s, 3H, 4-CH₃), 2.15-2.20 (m, 1H, CH₂), 2.54-2.70 (m, 3H, CH₂), 3.79 (s, 3H, OCH₃), 5.36 (d, 1H, J 10.7, 1'-H), 6.19 (t, 1H, J 6.7, 5'-H), 6.79-6.84 (m, 1H, 2'-H), 6.86 (d, 2H, J 8.7, Ar-H), 6.99 (d, 2H, J 8.7, Ar-H), 7.35-7.45 (5H, m, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.1 (4-CH₃), 29.8 (CH₂), 30.4 (CH₂), 55.4 (OCH₃), 84.9 (C5'), 100.7 (C1'), 114.4 (Ar-C), 117.4 (CN), 118.5 (C5), 122.5 (Ar-C), 128.9, 129.0, 129.8, 130.2 (Ph-C and Ar-C), 133.7 (C4), 136.2 (Ph-C), 154.5 (C2'), 159.8 (Ar-C), 178.5 (C2).

4.2.4. 3-[1'-(Methoxycarbonyl)hex-1'-en-5'-oxy]-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1c). Methyl 6-chlorohept-2enoate: According to 4.2.1 from methyl 6-hydroxyhept-2-enoate (1.11 g, 6.95 mmol), PPh₃ (2.37 g, 9.03 mmol) and CCl₄ (8 mL). Reaction time: 3 h. Eluent used for chromatography: pentane/ $Et_2O=1:1$ (v/v). Yield: 731 mg (4.14 mmol, 60%), pale yellow oil, R_f 0.58 [SiO₂, pentane/Et₂O=1:1 (v/v)]. ¹H NMR (CDCl₃, 200 MHz) δ 1.52 (d, 3H, J 6.6, 7-H), 1.79–1.90 (m, 2H, CH₂), 2.25–2.55 (m, 2H, CH₂), 3.72 (s, 3H, OCH₃), 3.92-4.09 (m, 1H, 6-H), 5.87 (d, 1H, J 15.6, 2-H), 6.94 (dt, 1H, J_d 15.6, J_t 7.0, 3-H). ¹³C NMR (CDCl₃, 150 MHz) δ 25.3 (C7), 29.2 (CH₂), 38.3 (CH₂), 51.5 (OCH₃), 57.5 (C6), 12.8 (C2), 147.6 (C3), 166.9 (C=O). 3-[1'-(Methoxycarbonyl)hex-1'-en-5'-oxy]-5-(p*methoxyphenyl*)-4-*methylthiazole*-2(3H)-*thione* (1c): According to 4.2.1 from methyl 6-chlorohept-2-enoate (731 mg, 4.14 mmol), 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt (1.58 g, 4.14 mmol) and DMF (8.5 mL). Reaction time: 6 days. The reaction mixture was treated with CH₂Cl₂ (40 mL) and H₂O (40 mL). The layers were separated and the organic layer was kept. The aqueous layer was extracted with CH₂Cl₂ (3×40 mL). Eluent used for chromatography: pentane/EtOAc=1:1 (v/v). Yield: 452 mg (1.15 mmol, 49%), pale yellow oil, R_f 0.62 [SiO₂, pentane/EtOAc=1:1 (v/v)]. UV (MeOH) λ_{max} (lg e/m^2 mol⁻¹)= 332 nm (3.00). ¹H NMR (CDCl₃, 200 MHz) δ 1.32 (d, 3H, *J* 6.3, 6'-H), 1.72–2.02 (m, 1H, CH₂), 2.28 (s, 3H, 4-CH₃), 2.45–2.56 (m, 2H CH₂), 3.72 (s, 3H, COOCH₃), 3.83 (s, 3H, OCH₃), 5.39–5.55 (m, 1H, 5'-H), 5.89 (d, 1H, *J* 15.7, 1'-H), 6.94 (d, 2H, *J* 8.7, Ar–H), 6.94–7.09 (m, 1H, 2'-H), 7.24 (d, 2H, *J* 7.6, Ar–H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.7 (4-CH₃), 18.4 (C6'), 28.0 (CH₂), 33.3 (CH₂), 51.4 (OCH₃), 55.4 (OCH₃), 80.7 (C5'), 114.5 (Ar–C), 119.4 (C5), 121.4 (C1'), 122.5 (Ar–C), 129.8 (Ar–C), 133.3 (C4), 148.1 (C2'), 159.9 (Ar–C), 166.9 (C=O), 179.1 (C2).

4.2.5. 3-(1'-Methoxycarbonyl-5'-phenylpent-1'-en-5'-oxy)-5-(pmethoxyphenyl)-4-methylthiazole-2(3H)-thione (1d). Methyl 6chloro-6-phenylhex-2-enoate: According to 4.2.1 from methyl 6hydroxy-6-phenylhex-2-enoate (2.91 g, 13.21 mmol), PPh₃ (4.50 g, 17.17 mmol) and CCl₄ (15 mL). Reaction time: 3 h. Eluent used for chromatography: pentane/Et₂O=1:1 (v/v). Yield: 2.53 g [10.60 mmol, 80%, (*E*)/(*Z*)=91:9], pale yellow oil, *R*_f 0.92 [SiO₂, pentane/Et₂O=1:1 (v/v)]. UV (CHCl₃) λ_{max} (lg ε/m^2 mol⁻¹)=338 nm (3.17), 240 nm (3.12). (*E*)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 2.14–2.42 (m, 4H, CH₂), 3.73 (s, 3H, OCH₃), 4.83–4.85 (m, 1H, 6-H), 5.86 (d, 1H, J 15.5, 2-H), 6.94 (dt, 1H, J_d 15.7, J_t 6.8, 3-H), 7.30–7.33 (m, 1H, Ph–H), 7.35–7.37 (m, 4H, Ph-H). ¹³C NMR (CDCl₃, 150 MHz) δ 29.5 (CH₂), 38.0 (CH₂), 51.5 (OCH₃), 62.5 (C6), 122.0 (C2), 126.8, 128.4, 128.7, 141.1 (Ph-C), 147.1 (C3), 166.8 (C=O), (Z)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 2.14-2.42 (m, 4H, CH₂), 3.74 (s, 3H, OCH₃), 4.83–4.85 (m, 1H, 6-H), 5.91 (d, 1H, J 15.8, 2-H), 7.05 (dt, 1H, Jd 15.7, Jt 6.5, 3-H), 7.30–7.33 (m, 1H, Ph–H), 7.35-7.37 (m, 4H, Ph-H). ¹³C NMR (CDCl₃, 150 MHz) δ 29.5 (CH₂), 35.2 (CH₂), 51.5 (OCH₃), 62.5 (C6), 121.8 (C2), 126.8, 128.4, 128.7, 141.1 (Ph-C), 146.8 (C3), 166.8 (C=O). 3-(1'-Methoxycarbonyl-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1d): According to 4.2.1 from methyl 6-chloro-6-phenylhex-2enoate (2.53 g, 10.60 mmol), 3-hydroxy-5-(p-methoxyphenyl)-4methylthiazole-2(3H)-thione tetraethylammonium salt (4.06 g, 10.60 mmol) and DMF (21 mL). Reaction time: 10 days. The reaction mixture was treated with CH₂Cl₂ (100 mL) and H₂O (100 mL). The layers were separated and the organic layer was kept. The aqueous layer was extracted with CH₂Cl₂ (3×50 mL). The product was crystallized from Et₂O/pentane. Yield: 3.38 g (7.42 mmol, 70%), pale yellow solid, $R_f 0.42$ [SiO₂, pentane/Et₂O=1:1 (v/v)]. ¹H NMR (CDCl₃, 600 MHz) § 1.53 (s, 3H, 4-CH₃), 2.17-2.23 (m, 1H, CH₂), 2.40-2.46 (m, 1H, CH₂), 2.51–2.63 (m, 2H, CH₂), 3.73 (s, 3H, COOCH₃), 3.79 (s, 3H, OCH3), 5.89 (d, 1H, J 15.6, 1'-H), 6.21 (t, 1H, J 7.0, 5'-H), 6.86 (d, 2H, J 8.7, Ar-H), 7.00 (d, 2H, J 8.7, Ar-H), 7.01-7.05 (m, 1H, 2'-H), 7.36–7.39 (m, 4H, Ph–H), 7.40–7.43 (m, 1H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) & 12.1 (4-CH₃), 28.5 (CH₂), 30.5 (CH₂), 51.5 (COOCH₃), 55.3 (OCH₃), 85.3 (C5'), 114.3 (Ar-C), 118.3 (C5), 121.5 (C1'), 122.6 (Ar-C), 128.8, 129.0, 129.7, 129.9, 133.7 (Ph-C and Ar-C), 136.4 (C4), 147.9 (C2'), 159.7 (Ar-C), 166.9 (C=O), 178.5 (C2). Anal. calcd. for C₂₄H₂₅NO₄S₂ (455.59): C, 63.27; H, 5.53; N, 3.07; S, 14.07; found: C, 63.20; H, 5.55; N, 3.12; S, 13.94.

4.2.6. 3-(1'-Cyano-1'-cyclopropyl-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1e**). 2-Cyclopropyl-6-chloro-6-phenylhex-2-enenitrile: According to 4.2.1 from 2-cyclopropyl-6-hydroxy-6-phenylhex-2-enenitrile (2.48 g, 10.91 mmol), PPh₃ (3.72 g, 14.18 mmol) and CCl₄ (12 mL). Reaction time: 2 h. Eluent used for chromatography: pentane/Et₂O=1:3 (v/v). Yield: 2.26 g [9.20 mmol, 84%, (*E*)/(*Z*)=63:37], yellow oil,*R*_f 0.53 [SiO₂, pentane/Et₂O=1:3 (v/v)]. (*E* $)-isomer: ¹H NMR (CDCl₃, 400 MHz) <math>\delta$ 0.65–0.69 (m, 1H, cyclopropyl), 0.72–0.80 (m, 2H, cyclopropyl), 0.85–0.89 (m, 1H, cyclopropyl), 1.22–1.23 (m, 1H,

cyclopropyl), 2.11–2.32 (m, 2H, CH₂), 2.38–2.55 (m, 2H, CH₂), 4.83-4.86 (m, 1H, 6-H), 6.17 (t, 1H, J 7.7, 3-H), 7.31-7.38 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 5.9, 6.4, 14.1 (cyclopropyl), 29.1 (CH₂), 38.8 (CH₂), 62.5 (C6), 115.5 (CN), 118.8 (C2), 126.8, 128.5, 128.8, 141.0 (Ph–C), 143.1 (C3). (Z)-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 0.65–0.69 (m, 1H, cyclopropyl), 0.72–0.80 (m, 2H, cyclopropyl), 0.85-0.89 (m, 1H, cyclopropyl), 1.48-1.56 (m, 1H, cyclopropyl), 2.11-2.32 (m, 2H, CH₂), 2.38-2.55 (m, 2H, CH₂), 4.83-4.86 (m, 1H, 6-H), 6.28 (t, 1H, / 7.7, 3-H), 7.31-7.38 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 5.9, 6.4, 9.4 (cyclopropyl), 26.0 (CH₂), 38.4 (CH₂), 62.5 (C6), 117.5 (CN), 119.3 (C2), 126.9, 128.6, 128.7, 140.9 (Ph-C), 144.4 (C3). 3-(1'-Cyano-1'-cyclopropyl-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)thione (1e): According to 4.2.1 from 2-cyclopropyl-6-chloro-6phenylhex-2-enenitrile (623 mg, 2.53 mmol), 3-hydroxy-5-(pmethoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt (968 mg, 2.53 mmol) and DMF (5 mL). Reaction time: 7 days. The reaction mixture was treated with Et₂O (20 mL) and H₂O (25 mL). The layers were separated and the organic layer was kept. The aqueous layer was extracted with Et₂O (3×25 mL). Eluent used for chromatography: pentane/ $Et_2O=1:2$ (v/v). Yield: 858 mg [1.85 mmol, 73%, (E)/(Z)=62:38], yellow oil, $R_f 0.41$ [SiO₂, pentane/Et₂O=1:2 (v/v)]. (E)-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 0.66–0.69 (m, 1H, cyclopropyl), 0.74–0.88 (m, 3H, cyclopropyl), 1.24-1.27 (m, 1H, cyclopropyl), 1.52 (s, 3H, 4-CH₃), 2.17-2.25 (m, 1H, CH₂), 2.52-2.65 (m, 3H, CH₂), 3.79 (s, 3H, OCH₃), 6.18-6.24 (m, 1H, 5'-H), 6.38-6.46 (m, 1H, 2'-H), 6.86 (d, 2H, [8.5, Ar-H), 7.00 (d, 2H, [8.8, Ar-H), 7.38-7.42 (m, 5H, Ph-H). 13 C NMR (CDCl₃, 100 MHz) δ 5.9, 6.3 (cyclopropyl), 12.1 (4-CH₃), 14.1 (cyclopropyl), 27.6 (CH₂), 31.1 (CH₂), 55.3 (OCH₃), 85.1 (C5'), 114.4 (Ar-C), 118.3 (CN), 118.4 (C5), 122.6 (C1'), 128.8, 129.1, 129.7, 130.0, 133.7 (Ph-C and Ar-C), 136.1 (C4), 144.0 (C2'), 159.7 (Ar–C), 178.5 (C2). (Z)-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 0.66–0.69 (m, 1H, cyclopropyl), 0.74–0.88 (m, 3H, cyclopropyl), 1.24-1.27 (m, 1H, cyclopropyl), 1.53 (s, 3H, 4-CH₃), 2.17-2.25 (m, 1H, CH₂), 2.52-2.65 (m, 3H, CH₂), 3.79 (s, 3H, OCH₃), 6.18-6.24 (m, 1H, 5'-H), 6.38-6.46 (m, 1H, 2'-H), 6.86 (d, 2H, J 8.5, Ar-H), 7.00 (d, 2H, / 8.8, Ar-H), 7.38-7.42 (m, 5H, Ph-H). ¹³C NMR (CDCl₃, 100 MHz) δ 5.9, 6.3, 9.4 (cyclopropyl), 12.1 (4-CH₃), 25.1 (CH₂), 31.1 (CH₂), 55.3 (OCH₃), 85.3 (C5'), 114.4 (Ar-C), 115.7 (CN), 118.7 (C5), 122.5 (C1'), 128.8, 129.0, 129.7, 130.1, 133.7 (Ph-C and Ar-C), 136.4 (C4), 145.3 (C2'), 159.7 (Ar-C), 178.5 (C2).

4.3. 3-Alkoxythiazole-2(3*H*)-thiones 1f-h and 1j from alcohols

4.3.1. General procedure. In an atmosphere of nitrogen (5.0-quality, purged through a tube filled with CaCl₂), a solution of PPh₃ (3.0 equiv), 3-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (1.5 equiv) and a dienol (1 equiv) in dry benzene (10 mL/mmol) was treated at 0 °C in a dropwise manner with diethyl azodicarboxylate (3.0 equiv). The solution was stirred for 48 h in the dark at 22 °C. The reaction mixture was treated with a 2 M aqueous solution of NaOH (20 mL/mmol). The layers were separated and the organic layer was kept. The aqueous layer was extracted with Et₂O (2×20 mL/mmol) and CH₂Cl₂ (2×20 mL/mmol). Combined organic solutions were washed with H₂O (20 mL/mmol) and dried (MgSO₄). The solvent was removed under reduced pressure and the residue purified by chromatography (SiO₂).

4.3.2. 3-(9'-Methyldeca-1',8'-dien-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1f** $). According to 4.3.1 from 9-methyldeca-1,8-dien-5-ol (500 mg, 2.97 mmol) and 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1.13 g, 4.46 mmol). Eluent used for chromatography: pentane/Et₂O=4:1 (v/v). Yield: 718 mg (1.78 mmol, 60%), pale yellow oil, <math>R_f$ 0.50 [SiO₂, pentane/Et₂O=4:1 (v/v)]. ¹H NMR (CDCl₃, 400 MHz) δ 1.61 (s, 3H, CH₃), 1.69 (s,

3H, CH₃), 1.69–1.86 (m, 4H, CH₂), 2.07–2.32 (m, 4H, CH₂), 2.28 (s, 3H, 4-CH₃), 3.83 (s, 3H, OCH₃), 4.98–5.13 (m, 3H, 1'-H and 8'-H), 5.31–5.37 (m, 1H, 5'-H), 5.80–5.90 (m, 1H, 2'-H), 6.93–6.96 (m, 2H, Ar–H), 7.23–7.26 (m, 2H, Ar–H). ¹³C NMR (CDCl₃, 100 MHz) δ 12.9 (4-CH₃), 17.9 (CH₃), 23.9 (CH₂), 25.8 (CH₃), 29.4 (CH₂), 31.6 (CH₂), 32.3 (CH₂), 55.6 (OCH₃), 84.7 (C5'), 114.7 (Ar–C), 115.2 (C1'), 119.3 (C5), 123.0 (Ar–C), 123.5 (C8'), 130.0, 131.7, 132.6 (C9'), 138.0 (C2'), 160.1 (Ar–C), 179.4 (C2).

4.3.3. 3-(1'-Methoxynona-1',8'-dien-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1g). According to 4.3.1 from 1methoxynona-1,8-dien-5-ol [580 mg, 3.40 mmol, (E)/(Z)=72:28] and 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1.29 g, 5.10 mmol). Eluent used for chromatography: pentane/ $Et_2O=1:1$ (v/v). The product was crystallized from pentane/ Et_2O . Yield: 921 mg [2.28 mmol, 67%, (E)/(Z)=80:20], colorless solid, R_f 0.35 [SiO₂, pentane/Et₂O=1:1 (v/v)]. Anal. calcd. for C₂₁H₂₇NO₃S₂ (405.58): C, 62.19; H, 6.71; N, 3.45; found: C, 62.13; H, 6.86; N, 3.44. (*E*)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.69–1.82 (m, 4H, CH₂), 2.05-2.27 (m, 4H, CH₂), 2.28 (s, 3H, 4-CH₃), 3.51 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 4.72-4.77 (m, 1H, 2'-H), 4.98-5.01 (m, 1H, 9'-H), 5.04-5.07 (m, 1H, 9'-H), 5.32-5.39 (m, 1H, 5'-H), 5.80-5.88 (m, 1H, 8'-H), 6.34 (d, 1H, J 12.6, 1'-H), 6.93-6.96 (m, 2H, Ar-H), 7.23-7.25 (m, 2H, Ar-H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.9 (4-CH₃), 23.6 (CH₂), 29.3 (CH₂), 31.4 (CH₂), 33.5 (CH₂), 55.5 (OCH₃), 56.1 (1'-OCH₃), 84.2 (C5'), 101.9 (C2'), 115.3 (C9'), 114.6 (Ar-C), 119.4, 122.8, 130.0, 133.6, 137.8 (C8'), 147.8 (C1'), 160.0 (Ar–C), 179.2 (C2). (Z)-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.69–1.82 (m, 4H, CH₂), 2.05–2.27 (m, 4H, CH₂), 2.28 (s, 3H, 4-CH₃), 3.57 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 4.33-4.37 (m, 1H, 2'-H), 4.98–5.01 (m, 1H, 9'-H), 5.04–5.07 (m, 1H, 9'-H), 5.32-5.39 (m, 1H, 5'-H), 5.80-5.88 (m, 1H, 8'-H), 5.89-5.90 (m, 1H, 1'-H), 6.93–6.96 (m, 2H, Ar–H), 7.23–7.25 (m, 2H, Ar–H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.9 (4-CH₃), 19.6 (CH₂), 29.3 (CH₂), 31.3 (CH₂), 32.0 (CH₂), 55.5 (OCH₃), 56.7 (1'-OCH₃), 84.7 (C5'), 105.3 (C2'), 115.1 (C9'), 114.6 (Ar-C), 119.3, 122.9, 130.0, 133.8, 138.0 (C8'), 147.0 (C1'), 160.0 (Ar-C), 179.2 (C2).

4.3.4. 3-(1'-Cyanonona-1',8'-dien-5'-oxy)-5-(p-methoxyphenyl)-4methylthiazole-2(3H)-thione (1h). According to 4.3.1 from 6hydroxydeca-2,9-dienenitrile [1.01 g, 6.09 mmol, (*E*)/(*Z*)=71:29] and 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (2.31 g, 9.14 mmol). Eluent used for chromatography: pentane/Et₂O=1:1 (v/v). The product was crystallized from pentane/ Et₂O. Yield: 1.53 g [3.82 mmol, 63%, (*E*)/(*Z*)=72:28], colorless solid, R_f 0.43 [SiO₂, pentane/Et₂O=1:1 (v/v)]. Anal. calcd. for C₂₁H₂₄N₂O₂S₂ (400.56): C, 62.97; H, 6.04; N, 6.99; found: C, 62.81; H, 6.08; N, 6.89. (*E*)-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.57–1.87 (m, 4H, CH₂), 2.05-2.09 (m, 2H, CH₂), 2.27 (s, 3H, 4-CH₃), 2.58-2.79 (m, 2H, CH₂), 3.84 (s, 3H, OCH₃), 4.99-5.01 (m, 2H, 9'-H), 5.36–5.45 (m, 2H, 1'-H and 5'-H), 5.74–5.84 (m, 1H, 8'-H), 6.76-6.83 (m, 1H, 2'-H), 6.93-6.97 (m, 2H, Ar-H), 7.23-7.26 (m, 2H, Ar-H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.8 (4-CH₃), 29.1 (CH₂), 29.2 (CH₂), 30.5 (CH₂), 31.4 (CH₂), 55.4 (OCH₃), 83.4 (C5'), 100.6 (C1'), 114.5 (Ar-C), 115.8 (C9'), 117.3 (CN), 119.6, 122.4, 129.9 (Ar-C), 133.2, 136.9 (C8'), 154.9 (C2'), 159.6 (Ar-C), 179.2 (C2). (Z)isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.57–1.87 (m, 4H, CH₂), 2.05–2.09 (m, 2H, CH₂), 2.27 (s, 3H, 4-CH₃), 2.58–2.79 (m, 2H, CH₂), 3.84 (s, 3H, OCH₃), 4.99–5.01 (m, 2H, 9'-H), 5.36–5.45 (m, 2H, 1'-H and 5'-H), 5.74-5.84 (m, 1H, 8'-H), 6.65-6.74 (m, 1H, 2'-H), 6.93–6.97 (m, 2H, Ar–H), 7.23–7.26 (m, 2H, Ar–H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.8 (4-CH₃), 27.3 (CH₂), 29.3 (CH₂), 30.7 (CH₂), 31.1 (CH₂), 55.4 (OCH₃), 83.4 (C5'), 100.2 (C1'), 114.5 (Ar-C), 115.8 (C9'), 117.3 (CN), 119.6, 122.4, 129.9 (Ar-C), 133.2, 137.0 (C8'), 154.2 (C2'), 159.6 (Ar-C), 179.2 (C2).

4.3.5. 3-(1'-Methoxycarbonyl-1'-acetylamino-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1***j*). In an atmosphere of nitrogen (5.0-quality, purged through a tube filled with CaCl₂), methyl (6S)-2-(acetylamino)-6-hydroxy-6phenylhex-2-enoate (496 mg, 1.79 mmol), diethylphosphinoethane (713 mg, 1.79 mmol) and 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (681 mg, 2.69 mmol) were dissolved in dry benzene (10 mL). Diethyl azodicarboxylate (655 mg. 3.76 mmol) was added to this solution at 0 °C in a dropwise manner. The resulting mixture was stirred for 18.5 h in the dark at 22 °C. The solution was treated with 2 M aqueous NaOH (20 mL) and CH₂Cl₂ (20 mL). The layers were separated and the organic layer was kept. The aqueous layer was extracted with CH₂Cl₂ (2×20 mL). Combined organic layers were washed with brine (2×20 mL) and concentrated under reduced pressure. The residue was purified by chromatography $[SiO_2, pentane/EtOAc=1:3 (v/v)]$. Yield: 291 mg (0.55 mmol, 31%), pale yellow solid, R_f 0.33 [SiO₂, pentane/EtOAc=1:3 (v/v)]. ¹H NMR (CDCl₃, 400 MHz) δ 1.55 (s, 3H, CH₃), 2.09 (s, 3H, 4-CH₃), 2.22–2.30 (m, 1H, CH₂), 2.42–2.53 (m, 2H, CH₂), 2.59–2.66 (m, 1H, CH₂), 3.78 (s, 3H, COOCH₃), 3.79 (s, 3H, OCH3), 6.24 (t, 1H, J 7.0, 5'-H), 6.75 (t, 1H, J 7.4, 2'-H), 6.86 (d, 2H, J 8.6, Ar-H), 6.98 (d, 2H, J 8.6, Ar-H), 7.20 (br s, 1H, NH), 7.34-7.39 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 12.2 (4-CH₃), 23.3 (CH₃), 25.2 (CH₂), 30.4 (CH₂), 52.4 (COOCH₃), 55.4 (OCH₃), 85.2 (C5'), 114.4 (Ar-C), 118.6 (C5), 122.5 (C1'), 126.1, 128.7, 129.2, 129.3, 130.0, 133.9 (Ph-C and Ar-C), 136.2 (C4), 137.3 (C2'), 159.3 (Ar-C), 165.0 (C=O), 168.9 (C=O), 178.3 (C2).

4.4. 3-Alkoxythiazole-2(3H)-thione 1i from alkenyl tosylates

4.4.1. 3-[1'-(Methoxvcarbonvl)nona-1'.8'-dien-5'-oxv]-5-(p-methoxvphenyl)-4-methylthiazole-2(3H)-thione (**1i**). A solution of 3-hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt (4.00 mmol) in dry DMF was treated in an atmosphere of nitrogen (5.0-quality, purged through a tube filled with CaCl₂) with (E)-1-(methoxycarbonyl)nona-1,8-dien-5-yl ptoluene sulfonate (1.41 g, 4.00 mmol) and stirred for 3 days in the dark at 22 °C. The reaction mixture was treated with H₂O (50 mL) and Et₂O (30 mL). The layers were separated and the organic layer was kept. The aqueous layer was extracted with Et_2O (2×30 mL). Combined organic layers were washed with a 2 M aqueous solution of NaOH (2×20 mL) and with brine (20 mL). The organic solution was dried (MgSO₄) and the solvent was removed under reduced pressure. The residue was purified by chromatography [SiO₂, pentane/Et₂O=1:1 (v/v)] and then crystallized from pentane/Et₂O. Yield: 844 mg (1.95 mmol, 49%), colorless solid, Rf 0.24 [SiO₂, pentane/Et₂O=1:1 (v/v)]. ¹H NMR (CDCl₃, 600 MHz) δ 1.73–1.93 (m, 4H, CH₂), 2.16–2.33 (m, 5H, 4-CH₃ and CH₂), 2.47–2.50 (m, 2H, CH₂), 3.73 (s, 3H, COOCH₃), 3.84 (s, 3H, OCH₃), 5.00-5.07 (m, 2H, 9'-H), 5.38-5.40 (m, 1H, 5'-H), 5.78-5.89 (m, 2H, 1'-H and 8'-H), 6.94-7.02 (m, 3H, 2'-H and Ar-H), 7.24-7.25 (m, 2H, Ar-H). ¹³C NMR (CDCl₃, 150 MHz) δ 12.8 (4-CH₃), 27.9 (CH₂), 29.3 (CH₂), 30.7 (CH₂), 31.3 (CH₂), 51.5 (COOCH₃), 55.4 (OCH₃), 83.8 (C5'), 114.6, 115.6 (C9'), 119.3, 121.5 (C1'), 122.6, 129.9, 133.3, 137.3 (C8'), 148.2 (C2'), 156.0 (Ar-C), 167.0 (C=O), 179.2 (C2). Anal. calcd. for C₂₂H₂₇NO₄S₂ (433.58): C, 60.94; H, 6.28; N, 3.23; found: C, 60.52; H, 6.14; N 3.60.

4.5. Conversion of 3-alkoxythiazolethiones 1a—e and 1j with Bu₃SnH or Bu₃SnD

4.5.1. General procedure. To a solution of 3-alkoxylthiazole-2(3*H*)thione **1** (1 equiv, c^0 =50 mM) in deaerated benzene was added Bu₃SnH or Bu₃SnD (3.7 equiv, c^0 =185 mM). The solution was photolyzed for 1.5 h. The solvent was removed under reduced pressure and the residue was purified by chromatography (SiO₂).

4.5.2. Conversion of **1a** with Bu₃SnH. According to 4.5.1 from 3-(1'-cyanohex-1'-en-5'-oxy)-5-(*p*-methoxyphenyl)-4-methylthiazole-

2(3H)-thione (1a) (252 mg, 0.70 mmol) and Bu₃SnH (754 mg, 0.69 mL, 2.59 mmol) in benzene (14 mL). Eluent used for chromatography: CH₂Cl₂. (5-Methyltetrahydrofuran-2-yl)acetonitrile (**5a**): Yield: 61 mg (0.48 mmol, 69%, *cis/trans*=38:62), pale yellow oil, *R*_f 0.20 (SiO₂, CH₂Cl₂). HRMS: calcd. for C₇H₁₀NO [M⁺-H]: 124.0762; found: 124.0780. cis-isomer: MS (EI, 70 eV) m/z 124 (2), 110 (27), 85 (100), 82 (42), 80 (7), 67 (22), 57 (22), 55 (40). ¹H NMR (CDCl₃, 600 MHz) δ 1.26 (d, 3H, 16.2, CH₃), 1.51-1.62 (m, 1H, CH₂), 1.75-1.82 (m, 1H, CH₂), 2.00–2.05 (m, 1H, CH₂), 2.10–2.16 (m, 1H, CH₂), 2.51-2.61 (m, 2H, CH₂CN), 4.00-4.05 (m, 1H, 2-H), 4.09-4.13 (m, 1H, 5-H). ¹³C NMR (CDCl₃, 150 MHz) § 21.0 (CH₃), 24.6 (CH₂CN), 30.8 (CH₂), 32.6 (CH₂), 74.0 (C5), 76.6 (C2), 117.5 (CN). trans-isomer: MS (EI, 70 eV) m/z 124 (3), 110 (25), 85 (100), 82 (49), 80 (10), 67 (28), 57 (28), 55 (49). ¹H NMR (CDCl₃, 600 MHz) δ 1.22 (d, 3H, J 6.1, CH₃), 1.51–1.62 (m, 1H, CH₂), 1.75–1.82 (m, 1H, CH₂), 2.10–2.16 (m, 1H, CH₂), 2.19–2.24 (m, 2H, CH₂), 2.51–2.61 (m, 2H, CH₂CN), 4.20–4.28 (m, 2H, 2-H and 5-H). ¹³C NMR (CDCl₃, 150 MHz) δ 20.9 (CH₃), 24.3 (CH₂CN), 31.7 (CH₂), 33.6 (CH₂), 73.6 (C5), 76.1 (C2), 117.6 (CN).

4.5.3. Conversion of 1b with Bu₃SnH. According to 4.5.1 from 3-(1'cyano-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxylphenyl)-4-methylthiazole-2(3H)-thione (1b) (212 mg, 0.50 mmol) and Bu₃SnH (538 mg, 0.49 mL, 1.85 mmol) in benzene (10 mL). Eluent used for chromatography: CH₂Cl₂. (5-Phenyltetrahydrofuran-2-yl)acetonitrile (**5b**): Yield: 63 mg (0.34 mmol, 67%, *cis/trans*=44:56), pale yellow oil, *R*_f 0.30 (SiO₂, CH₂Cl₂). HRMS: calcd. for C₁₂H₁₃NO (M⁺): 187.0997; found: 187.0989. cis-isomer: MS (EI, 70 eV) m/z 186 (36), 147 (9), 144 (42), 129 (9), 120 (32), 117 (27), 115 (16), 105 (100), 91 (36), 77 (42), 51 (21). ¹H NMR (CDCl₃, 600 MHz) δ 1.92–2.00 (m, 2H, CH₂), 2.25–2.38 (m, 2H, CH₂), 2.63–2.76 (m, 2H, CH₂CN), 4.30–4.34 (m, 1H, 2-H), 4.92 (t, 1H, J 7.3, 5-H), 7.27–7.39 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 24.4 (CH₂CN), 30.9 (CH₂), 34.0 (CH₂), 74.2 (C5), 81.5 (C2), 117.4 (CN), 125.8, 127.6, 128.4, 141.5 (Ph-C). trans-isomer: MS (EI, 70 eV) m/z 186 (35), 147 (8), 144 (41), 129 (11), 120 (32), 117 (27), 115 (17), 105 (100), 91 (36), 77 (39), 51 (21). ¹H NMR (CDCl₃, 600 MHz) δ 1.92–2.00 (m, 2H, CH₂), 2.25–2.38 (m, 1H, CH₂), 2.45–2.49 (m, 1H, CH₂), 2.63–2.76 (m, 2H, CH₂CN), 4.46–4.50 (m, 1H, 2-H), 5.15 (t, 1H, / 7.2, 5-H), 7.27–7.39 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 24.4 (CH₂CN), 31.7 (CH₂), 35.0 (CH₂), 74.6 (C5), 82.0 (C2), 117.4 (CN), 125.5, 127.5, 128.4, 142.2 (Ph-C).

4.5.4. Conversion of 1b with Bu₃SnD. According to 4.5.1 from 3-(1'cyano-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxylphenyl)-4-methylthiazole-2(3H)-thione (1b) (211 mg, 0.50 mmol) and Bu₃SnD (540 mg, 0.49 mL, 1.85 mmol) in benzene (10 mL). Eluent used for chromatography: CH₂Cl₂. (5-Phenyltetrahydrofuran-2-yl)-2-d₁-acetonitrile (5b_{d1}): Yield: 69 mg (0.37 mmol, 74%, cis/trans=46:54), pale yellow oil, R_f 0.41 (SiO₂, CH₂Cl₂). cis-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.92–1.99 (m, 2H, CH₂), 2.25–2.38 (m, 2H, CH₂), 2.63–2.73 (m, 1H, CHCN), 4.30-4.33 (m, 1H, 2-H), 4.91 (t, 1H, J7.3, 5-H), 7.27-7.39 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 24.13 (t, ¹J_{C,D} 20.34, CHDCN), 30.8 (CH₂), 34.0 (CH₂), 74.2 (C5'), 82.0 (C2'), 117.4 (CN), 125.8, 127.6, 128.4, 141.6 (Ph–C). trans-isomer: ¹H NMR (CDCl₃, 600 MHz) δ 1.92–1.99 (m, 2H, CH₂), 2.25-2.38 (m, 1H, CH₂), 2.44-2.50 (m, 1H, CH₂), 2.63-2.73 (m, 1H, CHCN), 4.46-4.50 (m, 1H, 2-H), 5.14 (t, 1H, J7.2, 5-H), 7.27-7.39 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 24.13 (t, ¹J_{CD} 20.34, CHDCN), 31.7 (CH₂), 35.0 (CH₂), 74.5 (C5'), 81.4 (C2'), 117.4 (CN), 125.4, 127.5, 128.4, 142.2 (Ph-C).

4.5.5. Conversion of **1c** with Bu_3SnH . According to 4.5.1 from 3-[(1'-(methoxycarbonyl)hex-1'-en-5'-oxy)-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1c**) (249 mg, 0.63 mmol) and Bu_3SnH (678 mg, 0.62 mL, 2.33 mmol) in benzene (12.5 mL). Eluent used for chromatography: pentane/Et₂O=2:1 (v/v). *Methyl* (5-*methyltetrahydrofuran*-2-*yl*)*acetate* (**5c**): Yield: 68 mg (0.43 mmol, 68%, *cis/trans*=37:63), pale yellow oil, R_f 0.43 [SiO₂, pentane/

Et₂O=2:1 (v/v)]. cis-isomer: MS (EI, 70 eV) *m/z* 157 (1), 143 (9), 127 (4), 116 (63), 111 (15), 85 (89), 83 (30), 67 (22), 59 (37), 55 (100). HRMS: calcd. for C₈H₁₄O₃ [M⁺]: 158.0943; Found: 158.0950. ¹H NMR (CDCl₃, 400 MHz) & 1.19-1.23 (m, 3H, 5-CH₃), 1.42-1.53 (m, 1H, CH₂), 1.55–1.64 (m, 1H, CH₂), 1.94–2.08 (m, 2H, CH₂), 2.41–2.50 (m, 1H, CH₂COOCH₃), 2.57-2.66 (m, 1H, CH₂COOCH₃), 3.68 (s, 3H, OCH₃), 3.93–4.01 (m, 1H, 2-H), 4.19–4.26 (m, 1H, 5-H). ¹³C NMR (CDCl₃, 100 MHz) & 21.4 (5-CH₃), 31.2 (CH₂), 32.6 (CH₂), 41.0 (CH₂COOCH₃), 51.6 (OCH₃), 75.3 (C5), 75.7 (C2). trans-isomer: MS (EI, 70 eV) m/z 157 (2), 143 (6), 127 (6), 116 (56), 111 (14), 101 (14), 85 (82), 83 (30), 67 (23), 59 (41), 55 (100). HRMS: calcd. for C₈H₁₄O₃ [M⁺]: 158.0943; Found: 158.0947. ¹H NMR (CDCl₃, 400 MHz) δ 1.19-1.23 (m, 3H, 5-CH₃), 1.42-1.53 (m, 1H, CH₂), 1.55-1.64 (m, 1H, CH₂), 1.94–2.08 (m, 1H, CH₂), 2.10–2.19 (m, 1H, CH₂), 2.41–2.50 (m, 1H, CH₂COOCH₃), 2.57–2.66 (m, 1H, CH₂COOCH₃), 3.86 (s, 3H, OCH₃), 4.07–4.15 (m, 1H, 2-H), 4.37–4.44 (m, 1H, 5-H). ¹³C NMR (CDCl₃, 100 MHz) & 21.2 (5-CH₃), 32.1 (CH₂), 33.6 (CH₂), 40.8 (CH₂COOCH₃), 51.6 (OCH₃), 74.8 (C5), 75.0 (C2).

4.5.6. Conversion of 1d with Bu₃SnH. According to 4.5.1 from 3-(1'methoxycarbonyl-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1d) (319 mg, 0.70 mmol) and Bu₃SnH (754 mg, 0.69 mL, 2.59 mmol) in benzene (14 mL). Eluent used for chromatography: pentane/Et₂O=2:1 (v/v). Methyl (5-phenyltetrahydrofuran-2-yl)acetate (5d): Yield: 111 mg (0.50 mmol, 71%, cis/ trans=41:59), colorless oil, R_f 0.24 [SiO₂, pentane/Et₂O=2:1 (v/v)]. HRMS: calcd. for C₁₃H₁₆O₃ [M⁺]: 220.1099; found: 220.1105. cisisomer: MS (EI, 70 eV) m/z 220 (M⁺, 7), 219 (5), 147 (28), 129 (12), 120 (100), 117 (26), 105 (46), 91 (37), 77 (28), 55 (22). ¹H NMR (CDCl₃, 400 MHz) δ 1.71–1.80 (m, 1H, CH₂), 1.82–1.94 (m, 1H, CH₂), 2.16–2.43 (m, 2H, CH₂), 2.53-2.64 (m, 1H, CH₂COOCH₃), 2.71-2.82 (m, 1H, CH₂COOCH₃), 3.71 (s, 3H, OCH₃), 4.43-4.50 (m, 1H, 2-H), 4.91 (t, 1H, J 7.1, 5-H), 7.23–7.27 (m, 1H, Ph–H), 7.32–7.33 (m, 4H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) & 31.2 (CH₂), 34.3 (CH₂), 40.8 (CH₂COOCH₃), 51.7 (OCH₃), 75.8 (C5), 81.2 (C2), 125.7, 127.2, 128.3, 142.8 (Ph–C), 171.6 (C= O). trans-isomer: MS (EI, 70 eV) *m/z* 220 (M⁺, 6), 219 (3), 147 (24), 129 (12), 120 (100), 117 (22), 105 (43), 91 (32), 77 (22), 55 (16). ¹H NMR (CDCl₃, 400 MHz) δ 1.71–1.80 (m, 1H, CH₂), 1.82–1.94 (m, 1H, CH₂), 2.16-2.43 (m, 2H, CH₂), 2.53-2.64 (m, 1H, CH₂COOCH₃), 2.71-2.82 (m, 1H, CH₂COOCH₃), 3.72 (s, 3H, OCH₃), 4.60-4.66 (m, 1H, 2-H), 5.04 (t, 1H, J 7.1, 5-H), 7.23-7.27 (m, 1H, Ph-H), 7.32-7.33 (m, 4H, Ph-H). ¹³C NMR (CDCl₃, 100 MHz) δ 32.1 (CH₂), 35.1 (CH₂), 40.7 (CH₂COOCH₃), 51.7 (OCH₃), 75.9 (C5), 80.5 (C2), 125.5, 127.1, 128.3, 143.3 (Ph-C), 171.7 (C=0).

4.5.7. Conversion of 1j with Bu₃SnH. According to 4.5.1 from 3-(1'methoxycarbonyl-1'-acetylamino-5'-phenylpent-1'-en-5'-oxy)-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1j**) (179 mg, 0.35 mmol) and Bu₃SnH (378 mg, 0.34 mL, 1.30 mmol) in benzene (7 mL). Eluent used for chromatography: pentane/EtOAc=1:3 (v/v). *rel-(2R,6R)-Methyl N-acetylamino-(5-phenyltetrahydrofuran-2-yl)* acetate rel-(2R,6R)-(5j): Yield: 18 mg (65.0 µmol, 19%, cis/ trans=32:68), pale yellow oil, Rf 0.45 [SiO₂, pentane/EtOAc=1:3 (v/ v)]. rel-(2R,5S,6R)-(5j) (cis-isomer): ¹H NMR (CDCl₃, 400 MHz) δ 1.76–1.87 (m, 2H, CH₂), 1.91 (s, 3H, CH₃), 2.06–2.08 (m, 1H, CH₂), 2.25–2.31 (m, 1H, CH₂), 3.72 (s, 3H, OCH₃), 4.50 (td, 1H, J_t 7.1, J_d 2.6, 2-H), 4.75 (dd, 1H, J 9.0, 2.6, 6-H), 4.83 (t, 1H, J 7.0, 5-H), 6.08 (d, 1H, J 8.8, NH), 7.16–7.32 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 23.1 (CH₃), 28.2 (CH₂), 33.5 (CH₂), 52.6 (OCH₃), 54.7 (C6), 79.2 (C5), 81.0 (C2), 125.6, 127.6, 128.5, 141.9 (Ph-C), 170.4 (C=O), 171.0 (C=O). rel-(2*R*,5*R*,6*R*)-(**5j**) (trans-isomer): ¹H NMR (CDCl₃, 400 MHz) δ 1.76–1.87 (m, 2H, CH₂), 2.05 (s, 3H, CH₃), 2.06–2.08 (m, 1H, CH₂), 2.25-2.31 (m, 1H, CH₂), 3.73 (s, 3H, OCH₃), 4.62 (td, 1H, Jt 7.3, Jd 2.5, 2-H), 4.71 (dd, 1H, J 8.8, 2.7, 6-H), 4.95 (t, 1H, J 7.0, 5-H), 6.31 (d, 1H, J 8.7, NH), 7.16–7.32 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 23.2 (CH₃), 29.0 (CH₂), 35.1 (CH₂), 52.6 (OCH₃), 54.8 (C6), 79.4 (C5), 81.8 (C2), 125.4, 127.4, 128.4, 142.7 (Ph–C), 170.6 (C=O), 171.1 (C=O). *rel-(2R,6S)-Methyl N-acetylamino-(5-phenyltetrahydrofuran-2-yl)* acetate rel-(2R,6S)-(5j): Yield: 53 mg (0.19 mmol, 54%, cis/ trans=28:72), pale yellow oil, Rf 0.37 [SiO₂, pentane/EtOAc=1:3 (v/v)]. rel-(2R,5S,6S)-(5j) (cis-isomer): ¹H NMR (CDCl₃, 400 MHz) δ 1.60–1.70 (m, 1H, CH₂), 1.97 (s, 3H, CH₃), 2.08–2.14 (m, 1H, CH₂), 2.16-2.22 (m, 2H, CH₂), 3.70 (s, 3H, OCH₃), 4.22-4.26 (m, 1H, 2-H), 4.75–4.78 (m, 2H, 5-H and 6-H), 6.55 (br s, 1H, NH), 7.17–7.28 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 23.1 (CH₃), 28.3 (CH₂), 34.3 (CH₂), 52.4 (OCH₃), 55.5 (C6), 80.0 (C5), 81.8 (C2), 125.6, 127.5, 128.3, 141.6 (Ph–C), 169.8 (C=O), 170.5 (C=O). *rel*-(2*R*,5*R*,6*S*)-(**5j**) (trans-isomer): ¹H NMR (CDCl₃, 400 MHz) δ 1.76–1.85 (m, 1H, CH₂), 1.98 (s, 3H, CH₃), 2.08–2.14 (m, 2H, CH₂), 2.24–2.32 (m, 1H, CH₂), 3.72 (s, 3H, OCH₃), 4.38 (td, 1H, J_t 7.1, J_d 4.6, 2-H), 4.70 (dd, 1H, J 8.6, 4.6, 6-H), 4.90 (t, 1H, J 7.1, 5-H), 6.55 (br s, 1H, NH), 7.17-7.28 (m, 5H, Ph-H). ¹³C NMR (CDCl₃, 100 MHz) & 23.1 (CH₃), 28.6 (CH₂), 34.5 (CH₂), 52.4 (OCH₃), 55.5 (C6), 80.6 (C5), 81.4 (C2), 125.5, 127.4, 128.3, 142.5 (Ph-C), 169.8 (C=0), 170.8 (C=0).

4.6. Conversion of 3-alkoxythiazolethiones 1d and 1e with $Br CCl_3$

4.6.1. Conversion of 1d. To a solution of 3-(1'-methoxycarbonyl-5'phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1d) (456 mg, 1.00 mmol) in deaerated benzene (12 mL) was added BrCCl₃ (1.98 g, 1.00 mL, 10.00 mmol) and AIBN (41 mg, 0.25 mmol). The reaction mixture was stirred for 3 h at 80 °C. The solvent was removed under reduced pressure and the residue was purified by chromatography. Rf 0.49 [SiO₂, pentane/ Et₂O=1:1 (v/v)]: Methyl 2-bromo-2-(5'-phenyltetrahydrofuran-2'-yl) acetate (**9d**)²⁴ [Yield: 62 mg (0.21 mmol, 21%, *cis/trans*=44:56) as a mixture of diastereomers Acis/trans and Bcis/trans] and 5-(p-methoxyphenyl)-4-methyl-2-(trichloromethylsulfanyl)thiazole (3b) [Yield: 106 mg (0.23 mmol, 30%)], yellow oil. Methyl 2-bromo-2-(5'-phenyltetrahydrofuran-2'-yl)acetate (9d): cis-isomer (diastereomer A and B): ¹H NMR (CDCl₃, 200 MHz) δ 1.82–2.09 (m, 2H, CH₂), 2.18-2.47 (m, 2H, CH₂), 3.79 and 3.82 (s, 3H, OCH₃), 4.23 (d, 1H, J 8.6, CHBr), 4.47-4.61 (m, 1H, 2'-H), 4.94-5.02 (m, 1H, 5'-H), 7.26-7.36 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 29.6, 29.8 (CH₂), 34.1, 35.0 (CH₂), 47.3, 48.6 (CHBr), 53.0 (OCH₃), 79.4, 79.5 (C2'), 82.0, 82.7 (C5'), 125.6, 125.7, 128.3 (2C), 129.0, 129.7, 141.79, 141.83 (Ph-C), 168.6, 168.9 (C=O). trans-isomer (diastereomer A and B): ¹H NMR $(CDCl_3, 200 \text{ MHz}) \delta 1.82 - 2.09 \text{ (m, 2H, CH}_2), 2.18 - 2.47 \text{ (m, 2H, CH}_2),$ 3.80 and 3.81 (s, 3H, OCH₃), 4.22 (d, 0.3H, J 8.7, A-CHBr), 4.38 (d, 0.7H, J 6.9, B-CHBr), 4.64-4.75 (m, 1H, 2'-H), 5.05-5.12 (m, 1H, 5'-H), 7.26–7.36 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 150 MHz) δ 30.0, 30.4 (CH₂), 34.9, 35.3 (CH₂), 47.6, 48.2 (CHBr), 53.0, 53.1 (OCH₃), 79.5, 79.7 (C2'), 81.7, 81.8 (C5'), 125.5, 125.6, 127.4, 127.5, 128.3 (2C), 142.22, 142.23 (Ph-C), 168.7, 169.0 (C=O). 5-(p-methoxyphenyl)-4-methyl-2-(trichloromethylsulfanyl)thiazole (3b): NMR data agreed with published values.⁵ $R_f 0.33$ [SiO₂, pentane/Et₂O=1:1 (v/v)]: Methyl 2-[5"-(p-methoxyphenyl)-4"-methyl-2"-(methylsulfanyl)-thiazole]-2-(5'-phenyltetrahydrofuran-2'-yl)acetate (8d): Yield: 282 mg (0.62 mmol, 62%, cis/trans=43:57) as a mixture of diastereomers A_{cis/trans} and B_{cis/trans}, yellow oil. cis-isomer (diastereomer A and B): ¹H NMR (CDCl₃, 200 MHz) δ 1.85–2.00 (m, 1H, CH₂), 2.09–2.33 (m, 3H, CH₂), 2.41 (s, 3H, 4"-CH₃), 3.79 (s, 3H, OCH₃), 3.84 (s, 3H, OCH₃), 4.36–4.40 (m, 1H, CHS), 4.63–4.87 (m, 1H, 2'-H), 4.90–5.01 (m, 1H, 5'-H), 6.91–6.91 (m, 2H, Ar–H), 7.26–7.32 (m, 7H, Ph–H and Ar–H). trans-isomer (diastereomer A and B): ¹H NMR (CDCl₃, 200 MHz) δ 1.85–2.00 (m, 1H, CH₂), 2.09–2.33 (m, 3H, CH₂), 2.41 (s, 3H, 4"-CH₃), 3.79 (s, 3H, OCH₃), 3.84 (s, 3H, OCH₃), 4.36-4.40 and 4.63-4.66 (m, 1H, CHS), 4.63-4.87 (m, 1H, 2'-H), 5.05-5.16 (m, 1H, 5'-H), 6.91–6.91 (m, 2H, Ar–H), 7.26–7.32 (m, 7H, Ph–H and Ar–H). cis- and trans-isomer (diastereomer A and B): ¹³C NMR (CDCl₃, 100 MHz) δ 15.9, 15.92, 16.1 (CH₃), 29.36, 29.43, 29.8, 30.0 (CH₂), 34.2, 34.4, 34.6, 34.9 (CH₂), 52.4, 52.5, 52.6 (CHS), 54.55, 54.6, 55.1, 55.2, 55.4, 55.6 (2× OCH₃), 78.5, 78.8, 79.2, 79.3 (C2'), 81.1, 81.5, 81.8, 82.1 (C5'), 113.97, 113.99, 114.2 (Ar–C), 121.2, 121.5, 123.5, 123.6 (C5''), 125.35, 125.4, 125.5, 125.6, 127.08, 127.09, 127.1, 127.2, 127.8, 128.07, 128.1, 128.2, 128.5 (Ph–C), 130.1, 130.3 (Ar–C), 133.02, 133.06, 134.05, 134.1 (Ar–C), 141.6, 142.0, 142.4, 142.6 (Ar–C), 147.1, 147.2, 147.57, 147.6 (C4''), 155.87, 155.89, 157.4, 157.6 (C2''), 159.16, 159.2, 159.8 (Ar–C), 170.1, 170.2 (C=O).

4.6.2. Conversion of 1e. To a solution of 3-(1'-cyano-1'-cyclopropyl-5'-phenylpent-1'-en-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1e) (467 mg, 1.01 mmol) in deaerated benzene (20 mL) was added BrCCl₃ (2.00 g, 1.00 mL, 10.10 mmol). The solution was photolyzed for 1.5 h. The solvent was removed under reduced pressure and the residue was purified by chromatography. R_f 0.31 [SiO₂, pentane/Et₂O=3:1 (v/v)]: 5-bromo-2-(trans-5'-phenvltetrahydrofuran-2'-vl)-pent-2-enenitrile trans- (5ε) [Yield: 43 mg (0.14 mmol, 17% with respect of converted 1e)], 2-cyclopropyl-6-oxo-6-phenylhex-2-enenitrile (10) [Yield: 14 mg (0.06 mmol, 7% with respect of converted 1e)] and 5-(p-methoxyphenyl)-4-methyl-2-(trichloromethylsulfanyl)-thiazole (3b) [Yield: 124 mg (0.35 mmol, 41% with respect of converted 1e)], yellow oil. 5-Bromo-2-(trans-5'phenyltetrahydrofuran-2'-yl)-pent-2-enenitrile trans-(5ϵ): ¹H NMR (CDCl₃, 400 MHz) δ 1.91–2.00 (m, 1H, CH₂), 2.06–2.16 (m, 1H, CH₂), 2.33-2.42 (m, 1H, CH₂), 2.43-2.50 (m, 1H, CH₂), 2.96-3.00 (m, 2H, CH₂), 3.47 (t, 2H, / 6.5, CH₂Br), 4.78 (t, 1H, / 7.0, 2'-H), 5.16-5.19 (m, 1H, 5'-H), 6.54 (t, 1H, J 7.2, 3-H), 7.27–7.43 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 30.0, 32.1, 33.7, 34.7 (CH₂), 79.3 (C2'), 81.8 (C5'), 115.7 (CN), 120.1 (C2), 125.5, 127.6, 128.4, 142.1 (Ph-C), 143.5 (C3). 2-Cyclopropyl-6-oxo-6-phenylhex-2-enenitrile (10): ¹H NMR (CDCl₃, 400 MHz) δ 0.69-0.90 (m, 4H, cyclopropyl), 1.50-1.57 (m, 1H, cyclopropyl), 2.74-2.80 (m, 2H, CH₂), 3.15 (t, 2H, J 6.9, CH₂), 6.37 (t, 1H, J 7.6, 3-H), 7.45–7.49 (m, 2H, Ph–H), 7.56–7.60 (m, 1H, Ph–H), 7.95–7.97 (m, 2H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) δ 5.9, 14.1 (cyclopropyl), 25.7, 37.3 (CH₂), 115.7 (CN), 118.5 (C2), 128.0, 128.7, 133.3, 136.5 (Ph-C), 143.9 (C3), 198.2 (C=O). 5-(p-Methoxyphenyl)-4-methyl-2-(trichloromethylsulfanyl)-thiazole (**3b**): NMR data agreed with published values.⁵ $R_f 0.28-0.15$ [SiO₂, pentane/Et₂O=3:1 (v/ v)]: 5-bromo-2-(5'-phenyltetrahydrofuran-2'-yl)-pent-2-enenitrile (5ϵ) [Yield: 73 mg (0.24 mmol, 29% with respect of converted 1e, *cis*/ trans=18:82) and 2-cyclopropyl-6-oxo-6-phenylhex-2-enenitrile (10) [Yield: 16 mg (0.13 mmol, 9% with respect of converted **1e**, (E)/(Z)= 58:42)], yellow oil. 5-Bromo-2-(5'-phenyltetrahydrofuran-2'-yl)pent-2-enenitrile (5ε): cis-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.90–2.00 (m, 1H, CH₂), 2.07–2.16 (m, 1H, CH₂), 2.32–2.41 (m, 1H, CH₂), 2.43–2.52 (m, 1H, CH₂), 2.96–3.01 (m, 2H, CH₂), 3.48 (t, 2H, J 6.5, CH₂Br), 4.61 (t, 1H, / 6.4, 2'-H), 4.92-4.96 (m, 1H, 5'-H), 6.54 (t, 1H, J 7.4, 3-H), 7.27–7.43 (m, 5H, Ph–H). ¹³C NMR (CDCl₃, 100 MHz) 30.0, 31.6, 33.8, 34.7 (CH2), 79.0 (C2'), 82.3 (C5'), 117.4 (CN), 119.8 (C2), 126.1, 127.8, 128.5, 141.2 (Ph-C), 145.1 (C3). trans-isomer: NMR data agreed with values from an authentic sample. 2-Cyclopropyl-6oxo-6-phenylhex-2-enenitrile (**10**): ¹H NMR data agreed with values from an authentic sample. ¹³C NMR (CDCl₃, 100 MHz) 5.8, 6.4, 9.3, 14.1 (cyclopropyl), 22.9, 25.7 (CH₂), 36.9, 37.3 (CH₂), 115.7, 155.8 (CN), 118.5, 118.9 (C2), 127.95, 128.0, 128.68, 128.7, 133.3, 133.4, 136.48, 136.5 (Ph-C), 143.9, 144.3 (C3), 198.1, 198.2 (C=O). Rf 0.13 [SiO₂, pentane/Et₂O=3:1 (v/v)]: 5-bromo-2-(cis-5'-phenyltetrahydrofuran-2'-yl)-pent-2-enenitrile (5 ϵ) [Yield: 41 mg (0.13 mmol, 16% with respect of converted 1e)] and 3-(1'-cyano-1'-cyclopropyl-5'phenylpent-1'-en-5'-oxy)-5-(4-methoxyphenyl)-4-methylthiazole -2(3H)-thione (1e) [Yield: 76 mg (0.16 mmol, 16%)], yellow oil. 5-Bromo-2-(cis-5'-phenyltetrahydrofuran-2'-yl)-pent-2-enenitrile cis-(5ε): NMR data agreed with values from an authentic sample. 3-(1'cyano-1'-cyclopropyl-5'-phenylpent-1'-en-5'-oxy)-5-(4-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1e**): NMR data agreed with values from 4.2.6.

4.7. Conversion of 3-alkoxythiazolethiones 1f-i with Bu_3SnH or Bu_3SnD

4.7.1. General procedure. To a solution of 3-alkoxythiazole-2(3*H*)thione **1** (1 equiv, c^0 =55 mM) in deaerated benzene was added Bu₃SnH or Bu₃SnD (3.7 equiv, c^0 =205 mM). The solution was photolyzed for 45 min. The solvent was removed under reduced pressure and the residue was purified by chromatography (SiO₂).

4.7.2. Conversion of 1f with Bu₃SnH. According to 4.7.1 from 3-(9'methyldeca-1',8'-dien-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1f) (202 mg, 500 µmol), Bu₃SnH (540 mg, 0.49 mL, 1.85 mmol) and benzene (9 mL). Eluent used for chromatography: pentane/Et₂O=3:1 (v/v). 2-(But-3'-en-1'-yl)-5-(1"methylethyl)-tetrahydrofuran (5f): Yield: 79 mg (466 µmol, 93%, cis/ trans=32:68), colorless oil, R_f 0.69 [SiO₂, pentane/Et₂O=3:1 (v/v)]. cis-isomer: MS (EI, 70 eV) m/z 168 (M⁺, 0.4), 125 (92), 113 (14), 97 (33), 95 (78), 81 (84), 55 (100). ¹H NMR (CDCl₃, 400 MHz) δ 0.84 (d, 3H, J 6.6, CH₃), 0.95 (d, 3H, J 6.6, CH₃), 1.42-2.17 (m, 9H, CH and CH₂), 3.48-3.54 (m, 1H, 5-H), 3.78-3.93 (m, 1H, 2-H), 4.92-5.04 (m, 2H, 4'-H), 5.78–5.89 (m, 1H, 3'-H). ¹³C NMR (CDCl₃, 100 MHz) δ 18.5 (CH₃), 19.5 (CH₃), 28.5 (CH₂), 30.6 (CH₂), 31.3 (CH₂), 33.4 (CH), 35.4 (CH₂), 78.8 (C2), 84.9 (C5), 114.4 (C4'), 138.9 (C3'). transisomer: MS (EI, 70 eV) m/z 168 (M⁺, 3), 125 (90), 113 (14), 97 (34), 95 (77), 81 (88), 55 (100). ¹H NMR (CDCl₃, 400 MHz) δ 0.84 (d, 3H, / 6.6, CH₃), 0.95 (d, 3H, / 6.6, CH₃), 1.42-2.17 (m, 9H, CH and CH₂), 3.58-3.64 (m, 1H, 5-H), 3.78-3.93 (m, 1H, 2-H), 4.92-5.04 (m, 2H, 4'-H), 5.78–5.89 (m, 1H, 3'-H). ¹³C NMR (CDCl₃, 100 MHz) δ 18.4 (CH₃), 19.5 (CH₃), 29.6 (CH₂), 30.6 (CH₂), 32.5 (CH₂), 33.4 (CH), 35.3 (CH₂), 78.5 (C2), 84.2 (C5), 114.5 (C4'), 138.8 (C3').

4.7.3. Conversion of 1g with Bu₃SnH. According to 4.7.1 from 3-(1'methoxynona-1',8'-dien-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1g) (292 mg, 719 µmol), Bu₃SnH (774 mg, 0.70 mL, 2.66 mmol) and benzene (13 mL). Eluent used for chromatography: pentane/Et₂O=2:1 (v/v). 2-(But-3'-en-1'-yl)-5-(methoxymethyl)-tetrahydrofuran (5g): Yield: 114 mg (670 µmol, 93%, *cis/trans*=35:65), colorless oil, *R*_f 0.44 [SiO₂, pentane/Et₂O=2:1 (v/v)]. MS (EI, 70 eV) m/z 170 (M⁺, 0.04), 125 (58), 115 (7), 97 (15), 81 (64), 55 (100). cis-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.46–1.79 (m, 4H, CH₂), 1.89–2.18 (m, 4H, CH₂), 3.37–3.40 (m, 5H, OCH₃ and CH₂OCH₃), 3.82-3.89 (m, 1H, 5-H), 3.92-4.06 (m, 1H, 2-H), 4.92-5.04 (m, 2H, 4'-H), 5.77-5.88 (m, 1H, 3'-H). ¹³C NMR (CDCl₃, 100 MHz) & 28.0 (CH2), 30.3 (CH2), 30.6 (CH2), 35.0 (CH2), 59.2 (OCH₃), 75.8 (CH₂OCH₃), 77.8 (C5), 79.4 (C2), 114.3 (C4'), 138.5 (C3'). trans-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.46–1.79 (m, 4H, CH₂), 1.89–2.18 (m, 4H, CH₂), 3.37–3.40 (m, 5H, OCH₃ and CH₂OCH₃), 3.92-4.06 (m, 1H, 2-H), 4.12-4.19 (m, 1H, 5-H), 4.92-5.04 (m, 1H, 4'-H), 5.77–5.88 (m, 1H, 3'-H). $^{13}\mathrm{C}$ NMR (CDCl₃, 100 MHz) δ 28.5 (CH₂), 30.2 (CH₂), 31.6 (CH₂), 34.8 (CH₂), 59.2 (OCH₃), 75.6 (CH₂OCH₃), 77.2 (C5), 78.8 (C2), 114.3 (C4'), 138.5 (C3').

4.7.4. Conversion of **1h** with Bu_3SnH . According to 4.7.1 from 3-(1'-cyanonona-1',8'-dien-5'-oxy)-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1h**) (181 mg, 499 µmol), Bu_3SnH (540 mg, 0.49 mL, 1.85 mmol) and benzene (9 mL). Eluent used for chromatography: pentane/Et₂O=1:1 (v/v). [5-(*But-3'-en-1'-yl*)-*tetrahydro-furan-2-yl*]*acetonitrile* (**5h**) and 5'-[5-*methyltetrahydrofuran-2-yl*]*pent-2'-enenitrile* (**11h**): Yield: 75 mg [453 µmol, 91%, **5h** (*cis/trans*=38:62):**11h** (*cis/trans*=45:55)=51:49], colorless oil, *R_f* 0.28 [SiO₂, pentane/Et₂O=1:1 (v/v)]. ¹H NMR (CDCl₃, 400 MHz) δ 1.20–1.24 (m, 3H, CH₃-**11h**), 1.42–1.80 (m, 10H, CH₂), 1.95–2.51 (m, 6H, CH₂), 2.55–2.58 (m, 2H, CH₂CN-**5h**), 3.77–4.15 (m, 3H, 2-H and

5-H), 4.20–4.26 (m, 1H, 2-H and 5-H), 4.94–5.05 (m, 2H, 4'-H-5h), 5.29-5.36 (m, 1H, 2'-H-11h), 5.76-5.86 (m, 1H, 3'-H-5h), 6.50-6.57 [m, 0.46H, 3'-H-(Z)-11h], 6.71–6.78 [m, 0.54H, 3'-H-(E)-11h]. ¹³C NMR (CDCl₃, 100 MHz) δ 21.29 (CH₃-trans-**11h**), 21.41 (CH₃-cis-**11h**), 24.4 (CH₂CN-trans-5h), 24.6 (CH₂CN-cis-5h), 28.78, 28.81, 30.2, 30.3, 30.7, 30.8, 31.2, 31.3, 31.6, 31.8, 32.2, 32.3, 32.8, 33.88, 33.93, 34.03, 34.07, 34.47, 34.52, 34.8, 34.9 (CH₂), 73.7 (C2-trans-5h), 73.9 (C2-cis-5h), 74.75, 74.77, 75.5 (2C), 77.5, 77.8, 78.2, 78.4 [C2- and C5-cis/ trans-(E)/(Z)-11h], 79.6 (C5-trans-5h), 80.0 (C5-cis-5h), 99.5 [C2'-(E)/(Z)-11h], 99.9 [C2'-(E)/(Z)-11h], 114.8 (C4'-5h), 116.0 [CN-(E)/(Z)-11h], 117.6 [CN-(E)/(Z)-11h], 117.64 (CN-5h), 138.16 (C3'-trans-5h), 138.23 (C3'-cis-5h), 154.8, 155.0, 155.81, 155.83 [C3'-cis/trans-(E)/ (*Z*)-**11h**]. *v* (NaCl)/cm⁻¹1087, 1375, 1447, 1641, 1733, 2222, 2251, 2931. *cis/trans-(E)/(Z)-***11h**: MS (EI, 70 eV) *m/z* 165 (M⁺, 0.3), 164 (1), 150 (3), 136 (5), 120 (5), 108 (6), 85 (100). cis-**5h**: MS (EI, 70 eV) m/z 165 (M⁺, 0.2), 164 (1), 136 (13), 123 (26), 110 (100), 82 (43). trans-**5h**: MS (EI, 70 eV) m/z 165 (M⁺, 0.2), 164 (1), 136 (22), 123 (47), 110 (100), 82 (59). *cis/trans-(E)/(Z)*-**11h**: MS (EI, 70 eV) *m/z* 165 (M⁺, 0.2), 164 (1), 150 (3), 136 (2), 120 (3), 108 (5), 85 (100).

4.7.5. Conversion of **1h** with Bu₃SnD. According to 4.7.1 from 3-(1'cyanonona-1',8'-dien-5'-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (1h) (111 mg, 277 µmol), Bu₃SnD (297 mg, 0.27 mL, 1.02 mmol) and benzene (5 mL). Eluent used for chromatography: pentane/Et₂O=1:1 (v/v). [5-(But-3'-en-1'-yl)-tetrahydro*furan-2-yl*]*-2-d*₁*-acetonitrile* (5h_{d1}) and $5'-[5-methyl-d_1$ tetrahydrofuran-2-yl]-pent-2'-enenitrile (11h_{d1}): Yield: 42 mg [253 μ mol, 91%, **5h**_{d1} (*cis/trans*=34:66):**11h**_{d1} (*cis/trans*=45:55)= 53:47], colorless oil, $R_f 0.28$ [SiO₂, pentane/Et₂O=1:1 (v/v)].¹H NMR $(CDCl_3, 400 \text{ MHz}) \delta$ 1.19–1.24 (m, 2H, CH₂D-**11h_{d1}**), 1.42–1.82 (m, 8H, CH₂), 1.95-2.53 (m, 8H, CH₂), 2.54-2.58 (m, 1H, CHDCN-5h_{d1}), 3.77-4.15 (m, 3H, 2-H and 5-H), 4.20-4.26 (m, 1H, 2-H or 5-H), 4.94–5.04 (m, 2H, 4'-H-5h_{d1}), 5.29–5.36 (m, 1H, 2'-H-11h_{d1}), 5.75-5.87 (m, 1H, 3'-H-5h_{d1}), 6.50-6.57 [m, 0.47H, 3'-H-(Z)-11h_{d1}], 6.71-6.78 [m, 0.53H, 3'-H-(E)-11h_{d1}]. ¹³C NMR (CDCl₃, 100 MHz) δ 20.90 (t, ¹J_{CD} 18.96, CH₂D-trans-(E)/(Z)-**11h_{d1}**), 20.92 (t, ¹J_{CD} 18.96, CH_2D -trans-(E)/(Z)-11h_{d1}), 21.02 (t, ¹ J_{CD} 18.96, CH_2D -cis-11h_{d1}), 24.18 (t, ¹J_{C,D} 21.13, CHCDCN-trans-5h_{d1}), 24.39 (t, ¹J_{C,D} 21.13, CHCDCN-cis-5hd1), 28.79, 28.84, 30.2, 30.3, 30.7, 30.9, 31.3, 31.4, 31.6, 31.9, 32.5, 32.3, 32.9, 33.89, 33.94, 34.1, 34.2, 34.5, 34.6, 34.9, 35.0 (CH₂), 73.7 (C2-trans-5h_{d1}), 74.0 (C2-cis-5h_{d1}), 74.74, 74.76, 75.5 (2C), 77.6, 77.8, 78.3, 78.5 [C2- and C5-cis/trans-(E)/(Z)-11h_{d1}], 79.7 (C5-trans-5h_{d1}), 80.1 (C5-cis-5h_{d1}), 99.6 [C2'-(E)/(Z)-11h_{d1}], 100.0 [C2'-(E)/(Z)-11h_{d1}], 114.8 (C4'-5h_{d1}), 116.0 [CN-(E)/(Z)-11h_{d1}], 117.48 [CN-(E)/(Z)-11h_{d1}], 117.5 (CN-5h_{d1}), 138.2 (C3'-trans-5h_{d1}), 138.3 (C3'-cis-5h_{d1}), 154.95, 155.0, 155.76, 155.8 [C3'-cis/trans-(E)/(Z)-**11** h_{d1}]. ν (NaCl)/cm⁻¹ 1081, 1368, 1447, 1641, 2222, 2250, 2935. cis/trans-(E)/(Z)-11hd1: MS (EI, 70 eV) m/z 166 (M⁺, 0.4), 165 (1), 164 (0.3), 150 (3), 137 (5), 120 (5), 108 (6), 86 (100). cis-5hd1: MS (EI, 70 eV) *m*/*z* 166 (M⁺, 0.3), 165 (1), 137 (12), 124 (26), 111 (100), 83 (53). *trans*-**5h**_{d1}: MS (EI, 70 eV) *m*/*z* 166 (M⁺, 0.2), 165 (1), 137 (21), 124 (45), 111 (100), 83 (65). cis/trans-(E)/(Z)-11hd1: MS (EI, 70 eV) m/z 166 (M⁺, 0.3), 165 (1), 164 (0.3), 150 (3), 137 (2), 120 (5), 108 (3), 86 (100).

4.7.6. Conversion of **1i** with Bu_3SnD . According to 4.7.1 from 3-[1'-(methoxycarbonyl)nona-1',8'-dien-5'-oxy]-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1i**) (86 mg, 198 µmol), Bu_3SnD (214 mg, 0.19 mL, 733 µmol) and benzene (3.6 mL). Eluent used for chromatography: [SiO₂, pentane/Et₂O=1:1 (v/v)]. *Methyl* [5-(*but-3'-en-1'-yl*)-*tetrahydrofuran-2-yl*)-2-*d*₁-*acetate* (**5i**): Yield: 11 mg (57 µmol, 29%, *cis/trans*=35:65), colorless oil, R_f 0.28 [SiO₂, pentane/Et₂O=1:1 (v/v)]. ν (NaCl)/cm⁻¹ 1081, 1272, 1437, 1657, 1726, 2935. MS (EI, 70 eV) *m/z* 168 (2), 167 (1), 112 (6), 100 (13), 85 (100). cisisomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.20–1.73 (m, 4H, CH₂), 1.92–2.17 (m, 4H, CH₂), 2.41–2.46 (m, 1H, CHD), 3.68 (s, 3H, OCH₃), 3.82–3.88 (m, 1H, 5-H), 4.23 (q, 1H, J 6.6, 2-H), 4.92–5.03 (m, 2H, 4'-

H), 5.78–5.86 (m, 1H, 3'-H). ¹³C NMR (CDCl₃, 100 MHz) δ 30.3 (CH₂), 31.0 (CH₂), 31.8 (CH₂), 35.3 (CH₂), 40.73 (t, ¹J_{C,D} 20.34, CHD), 51.5 (OCH₃), 75.1 (C2), 79.2 (C5), 114.4 (C4'), 138.4 (C3'), 171.7 (C=O). NOESY (cross peaks) 2-H \leftrightarrow 5-H. trans-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.20–1.73 (m, 4H, CH₂), 1.92–2.17 (m, 4H, CH₂), 2.41-2.46 (m, 1H, CHD), 3.68 (s, 3H, OCH₃), 3.92-4.00 (m, 1H, 5-H), 4.25 (q, 1H, / 6.5, 2-H), 4.92-5.03 (m, 2H, 4'-H), 5.78-5.86 (m, 1H, 3'-H). ¹³C NMR (CDCl₃, 100 MHz) δ 30.3 (CH₂), 30.8 (CH₂), 31.6 (CH₂), 34.9 (CH₂), 40.45 (t, ¹J_{C,D} 20.34, CHD), 51.5 (OCH₃), 74.7 (C2), 78.5 (C5), 114.4 (C4'), 138.4 (C3'), 171.7 (C=O). NOESY (cross peaks) 5- $H \leftrightarrow 1'-H$. Methyl 5-[5'-methyl-d₁-tetrahydrofuran-2'-yl]-pent-2enoate (11i): Yield: 22 mg (108 µmol, 55%, cis/trans=39:61), colorless oil, *R*_f 0.22 [SiO₂, pentane/Et₂O=1:1 (v/v)]. v (NaCl)/cm⁻¹ 1081, 1272, 1437, 1657, 1726, 2935. MS (EI, 70 eV) m/z 170 (8), 157 (14), 144 (88), 125 (30), 117 (52), 112 (89), 55 (100). cis-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.17–1.25 (m, 2H, CH₂D), 1.47–1.77 (m, 4H, CH₂), 1.91-2.09 (m, 2H, CH₂), 2.21-2.38 (m, 2H, CH₂), 3.71 (s, 3H, OCH₃), 3.77-3.85 (m, 1H, 2'-H), 3.89-4.01 (m, 1H, 5'-H), 5.84 (m, 1H, 3-H), 6.95–7.02 (m, 1H, 4-H). ¹³C NMR (CDCl₃, 100 MHz) δ 21.09 (t, ¹J_{C,D} 19.43, CH₂D), 28.9 (CH₂), 31.2 (CH₂), 32.8 (CH₂), 34.5 (CH₂), 51.3 (OCH₃), 75.3 (C5), 78.5 (C2), 121.0 (C4'), 149.1 (C3'), 167.1 (C=O). trans-isomer: ¹H NMR (CDCl₃, 400 MHz) δ 1.17–1.25 (m, 2H, CH₂D), 1.47-1.77 (m, 4H, CH₂), 1.91-2.09 (m, 2H, CH₂), 2.21-2.38 (m, 2H, CH₂), 3.71 (s, 3H, OCH₃), 3.89-4.01 (m, 1H, 2-H), 4.04-4.10 (m, 1H, 5-H), 5.84 (m, 1H, 3'-H), 6.95–7.02 (m, 1H, 4'-H). ¹³C NMR (CDCl₃. 100 MHz) δ 20.8–21.3 (t, ¹J_{CD} 19.43, CH₂D), 29.0 (CH₂), 32.2 (CH₂), 33.8 (CH₂), 34.4 (CH₂), 51.3 (OCH₃), 74.5 (C5), 77.8 (C2), 121.0 (C4'), 149.1 (C3'), 167.1 (C=O).

Acknowledgements

This work was supported by the State of Rheinland-Pfalz (Graduiertenstipendium for A.G.) and is part of the Ph.D. theses of I.K. and A.G

Supplementary data

Instrumentation, reagent specification, preparation of alkenols, carbon-13 NMR-spectra of *N*-alkenoxythiazolethiones and tetrahydrofurans. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.08.083.

References and notes

- 1. Hartung, J.; Gottwald, T.; Špehar, K. Synthesis 2002, 1469-1498.
- Jones, M. J.; Moad, G.; Rizzardo, E.; Solomon, D. H. J. Org. Chem. 1989, 54, 1607–1611.

- Halliwell, B.; Gutteridge, J. M. C. Free Radicals in Biology and Medicine, 3rd ed.; Oxford University: Oxford, 1999, Chapter 2, pp 36–104.
- 4. Atkinson, R. Atmos. Environ. 2007, 41, 8468-8485.
- Hartung, J.; Schur, C.; Kempter, I.; Gottwald, T. Tetrahedron 2010, 66, 1365–1374.
- Hartung, J.; Kneuer, R.; Rummey, C.; Bringmann, G. J. Am. Chem. Soc. 2004, 126, 12121–12129.
- Schur, C.; Becker, N.; Bergsträßer, U.; Gottwald, T.; Hartung, J. Tetrahedron 2011, 67, 2338–2347.
- 8. Beckwith, A. L. J.; Hay, B. P. J. Am. Chem. Soc. 1988, 110, 4415-4416.
- 9. Bietti, M.; Lanzalunga, O.; Salamone, M. J. Org. Chem. 2005, 70, 1417–1422.
- Suárez, E. In Radicals in Organic Synthesis; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 440–454.
- 11. Wilsey, S.; Dowd, P.; Houk, K. N. J. Org. Chem. 1999, 64, 8801-8811.
- 12. Boto, A.; Gallardo, J. A.; Hernandez, D.; Hernandez, R. J. Org. Chem. 2007, 72, 7260–7269.
- 13. Hartung, J.; Gottwald, T. Tetrahedron Lett. 2004, 45, 5619–5621.
- 14. Schneiders, N.; Gottwald, T.; Hartung, J. Eur. J. Org. Chem. 2009, 797-800.
- Schur, C.; Kempter, I.; Hartung, J. Org. Synth. 2012, 89, in press.
 Rueda-Becerril, M.; Leung, J. C. T.; Dunbar, C. R.; Sammis, G. M. J. Org. Chem.
- **2011**, 76, 7720–7729. 17. Beckwith, A. L. J.; Hay, B. P.; Williams, G. M. J. Chem. Soc., Chem. Commun. **1989**, 1202–1203
- 18. Guindon, Y.; Denis, R. C. Tetrahedron Lett. 1998, 39, 339-342.
- 19. Arnone, M.; Hartung, J.; Engels, B. J. Phys. Chem. A 2005, 109, 5943-5950.
- 20. Giese, B. Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds;
- Pergamon: Oxford, 1986; Vol. 5.
 21. Bertrand, M. P.; Surzur, J. M.; Boyer, M.; Mihailović, M. L. Tetrahedron 1979, 35, 1365–1372
- 22. Rieke, R. D.; Moore, N. A. Tetrahedron Lett. 1969, 10, 2035-2038.
- Hartung, J.; Daniel, K.; Rummey, C.; Bringmann, G. Org. Biomol. Chem. 2006, 4, 4089–4100.
- 24. Schuch, D.; Fries, P.; Dönges, M.; Hartung, J. J. Am. Chem. Soc. 2009, 131, 12918–12920.
- Tanner, D. D.; Arhart, R. J.; Blackburn, E. V.; Das, N. C.; Wada, N. J. Am. Chem. Soc. 1974, 96, 829–834.
- 26. Herwig, K.; Lorenz, P.; Rüchardt, C. Chem. Ber. 1975, 108, 1421-1436.
- Hartung, J.; Daniel, K.; Bergsträßer, U.; Kempter, I.; Schneiders, N.; Danner, S.; Schmidt, P.; Svoboda, I.; Fuess, H. Eur. J. Org. Chem. 2009, 4135–4142.
- Rajan-Babu, T. V. In Handbook of Reagents for Organic Synthesis Reagents for Radical and Radical Ion Chemistry; Crich, D., Ed.; Wiley: Chichester, UK, 2008; pp 575–579.
- 29. Newcomb, M. Tetrahedron **1993**, 49, 1151–1176.
- 30. Hartung, J.; Hiller, M.; Schmidt, P. Liebigs Ann. 1996, 1425-1436.
- 31. Groß, A. Dissertation, TU Kaiserslautern, 2009, pp. 63-76.
- Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. J. Am. Chem. Soc. 1988, 110, 2565–2575.
- 33. Dowd, P.; Zhang, W. Chem. Rev. 1993, 93, 2091-2115.
- 34. Hartung, J.; Hiller, M.; Schmidt, P. Chem.-Eur. J. 1996, 2, 1014-1023.
- 35. Winkler, J. D.; Sridar, V. J. Am. Chem. Soc. 1986, 108, 1708-1709.
- 36. Hartung, J.; Gallou, F. J. Org. Chem. 1995, 60, 6706-6716.
- 37. Houk, K. N.; Munchausen, L. L. J. Am. Chem. Soc. 1976, 98, 937-946.
- 38. Anh, N. G. Frontier Orbitals; Wiley: Chichester, UK, 2007.
- 39. Giese, B.; He, J.; Mehl, W. Chem. Ber. 1988, 121, 2063-2066.
- 40. Heberger, K.; Fischer, H. Int. J. Chem. Kinet. **1993**, 25, 249–263.
- 41. Knühl, B.; Marque, S.; Fischer, H. Helv. Chim. Acta 2001, 84, 2290-2300.
- Kazmaier, U.; Pähler, S.; Endermann, R.; Häbich, D.; Kroll, H.-P.; Riedl, B. Bioorg. Med. Chem. 2002, 10, 3905–3913.
- Hartung, J.; Schwarz, M.; Svoboda, I.; Fuess, H.; Duarte, M. T. Eur. J. Org. Chem. 1999, 1275–1293.