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A Horner-Wittig Approach to *S,N*-Ketene Acetals

Acid-catalyzed hydrolysis of *S,N*-ketene acetals to (*S*)-thioesters

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Abstract: The synthesis of *S,N*-acetals of formyldiphenylphosphine oxide **2** is described. The stable lithiated anions of these acetals were applied in a Horner-Wittig reaction with several structural types of aldehydes. The resulting *S,N*-ketene acetals **1** were obtained in excellent yields. Ketones and pivaldehyde did not react with the sterically hindered phosphine oxide anions. *S,N*-ketene acetals **1** were found to be selectively hydrolyzed, under mildly acidic conditions, to the corresponding (*S*)-thioesters **5**. This, previously undescribed, reactivity of *S,N*-ketene acetals **1** allowed the two-step conversion of aldehydes into homologous (*S*)-thioesters **5** in good yields. Copyright © 1996 Elsevier Science Ltd

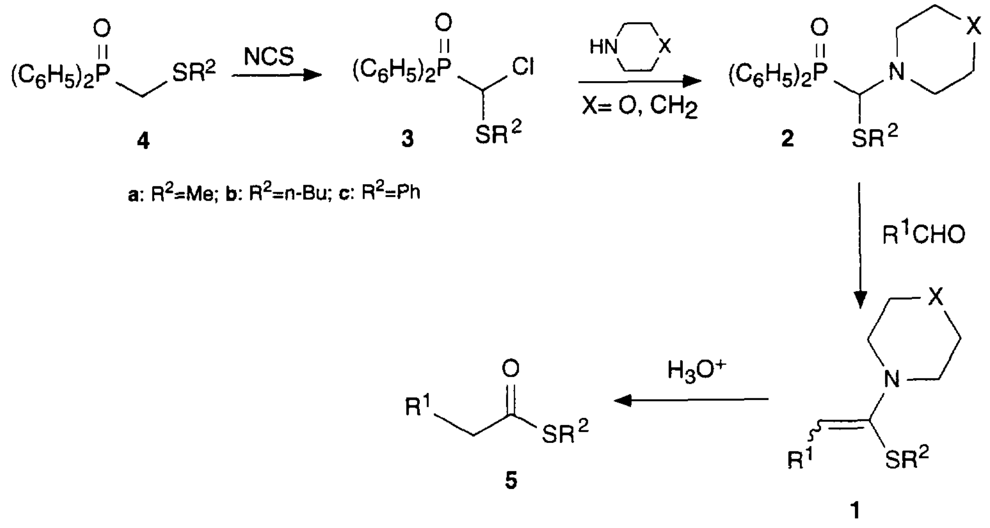
INTRODUCTION

Wittig reagents (phosphorus ylids), Horner-Wadsworth-Emmons (HWE) reagents [phosphoryl-stabilized carbanions, $(RO)_2P(=O)$], Horner-Wittig reagents [diphenylphosphinoyl-stabilized carbanions, $(C_6H_5)_2P(=O)$], and the Peterson olefination reaction, using sililated carbanions, all have been successfully applied to the conversion of aldehydes and ketones into their one-carbon-homologated *O,O*-[1], *S,S*-[2a-g], *O,S*-[2d,3] and *Se,Se*[2b,4]-ketene acetals. Application of any of these olefination methods to the synthesis of *S,N*-ketene acetals **1** has not been reported thus far. As early as 1969, Gross *et al*[5]. described the synthesis of *S,N*-acetals of formylphosphonates $(R^1O)_2P(O)CH(SR^2)NMe_2$, with R^1=Me, Et; R^2=Et, *n*-Bu. However, no further reports have appeared on the use of these potential HWE reagents for the synthesis of *S,N*-ketene acetals **1**.

The synthesis of an analogous phosphine oxide **2a**, X=O; R^2=Me (Scheme 1) was reported earlier by Broekhof *et al.*[6]. It was prepared by sulfenylation of the anion of 4-[(diphenylphosphinoyl)methyl]-morpholine with dimethyldisulfide. This compound could only be obtained analytically pure after tedious crystallization, leading to substantial loss of product.

Here, we report an alternative synthesis, leading to *S,N*-acetals of formyldiphenylphosphine oxide **2** in good yields and of high purity. A Horner-Wittig reaction with lithiated phosphine oxides **2** gave easy access to *S,N*-ketene acetals **1** (Scheme 1). A literature study revealed that a simple synthetic strategy for the synthesis of these compounds, using readily available starting materials, was not available[7a-c].

Phosphine oxides **2** were prepared by nucleophilic substitution of the chlorine atom in [(α-chloro)thiomethyl]diphenylphosphine oxides **3** by the secondary amines morpholine (X=O) and piperidine ($X=CH_2$) (Scheme 1).



Scheme 1.

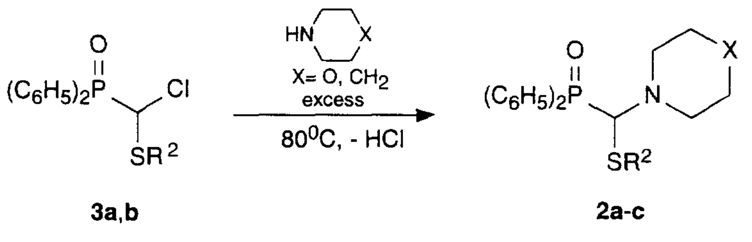
The synthesis of these α-chloro-substituted phosphine oxides **3** is described in detail elsewhere[8a,b]. They were obtained in nearly quantitative yields by chemo- and regioselective chlorination of (thiomethyl)diphenylphosphine oxides **4** with one equivalent of *N*-chlorosuccinimide (NCS) in dry chlorobenzene.

Surprisingly, the acid-catalyzed hydrolysis of *S,N*-ketene acetals appears not to have been reported previously. We found that *S,N*-ketene acetals **1**, R^1=alkyl, alkenyl, or aryl could be selectively hydrolyzed to the corresponding (*S*)-thioester **5** under mildly acidic conditions (Scheme 1).

RESULTS AND DISCUSSION

Synthesis of S,N-acetals of Formyldiphenylphosphine Oxide

The chlorine atom in [(α-chloro)thiomethyl]diphenylphosphine oxides **3** proved to be susceptible to nucleophilic substitution by secondary amines. Thus, by dissolving [(α-chloro)(alkylthio)-methyl]diphenylphosphine oxides **3a** (R^2=Me) and **3b** (R^2=*n*-Bu) in an excess of morpholine (X=O) or piperidine (X=CH_2) at 80°C, the chlorine atom was cleanly substituted by a morpholino or piperidino substituent. The desired phosphine oxides **2a-c** gradually precipitated during the course of the reaction.



(*1*)

After completion of the reaction, the white suspension was stirred in water in order to remove any excess of amine and liberated HCl; the latter as its ammonium salt. The work-up procedure was continued by filtration of the aqueous slurry and drying of the white residue. Phosphine oxides **2a-c** were purified for further use by crystallization.

Table 1. *S,N*-acetals of Formyldiphenylphosphine Oxide **2a-c**

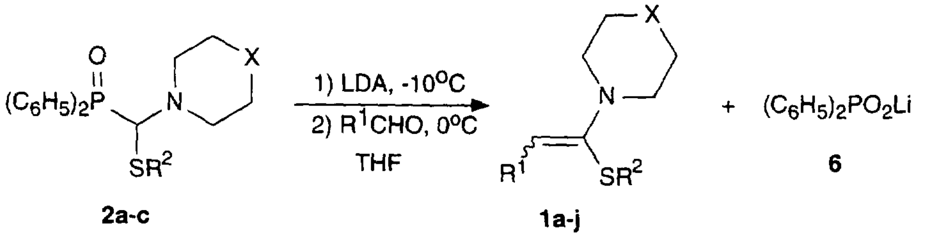
Compound	R^2	X	Yield (%)[a]	M.p. (°C)
2a	Me	O	70	146-8
2b	*n*-Bu	O	69	166-8
2c	Me	CH_2	72	192-5

[a] After crystallization.

For completion of the aminolysis of α-chlorinated phosphine oxides **3a** and **3b**, it is essential that the starting phosphine oxide dissolves in the amine. Even after prolonged reflux of a suspension of phosphine oxide **3a** in diethylamine (b.p. 55°C), the starting material was recovered unchanged. As a consequence, the preparation of *S,N*-acetals of formyldiphenylphosphine oxide **2**, at ambient pressure, is restricted to higher boiling amines like morpholine and piperidine. Attempted aminolysis of [(α-chloro)(phenylthio)-methyl]diphenylphosphine oxide **3c**, R^2=Ph failed; an intractable product mixture was obtained after work-up.

Horner-Wittig Synthesis of S,N-ketene Acetals

Phosphine oxides **2a** and **2c** showed poor solubility in THF. Nevertheless, sufficiently rapid deprotonation was achieved by treatment with LDA at temperatures between -10°C and 0°C. The resulting yellow anion solutions were stable for prolonged periods of time under these conditions. *n*-BuLi proved to be unsuitable for deprotonation of these phosphine oxides. This nucleophilic base led to products in which the *n*-butyl group had been incorporated. The lithiated anions of **2a-c** underwent an instantaneous Horner-Wittig reaction with aliphatic and aromatic aldehydes and cinnamaldehyde at 0°C (eq. 2).



(2)

Ketones (acetone, cyclohexanone and benzophenone), and pivaldehyde did not react. Eventually, acetone and cyclohexanone were deprotonated to the enolate by the lithiated phosphine oxide **2a** at ambient temperatures, as was judged from the disappearance of the characteristic intense yellow color of the anion solution. The starting phosphine oxide **2a** was recovered quantitatively. This lack of reactivity is not surprising, considering the steric hindrance between the tertiary substituted carbanionic center of **2a**-Li and the sterically shielded carbonyl group. Similar observations have been made in the case of lithiated carbanions derived from [1-(phenylthio)propyl]diphenylphosphine oxide[9a], $(C_6H_5)_2P(O)CH(SPh)C_2H_5$ and 4-[(diphenylphosphinoyl)phenylmethyl]morpholine[9b], $(C_6H_5)_2P(O)CHPh\overline{NCH_2CH_2OCH_2CH_2}$.

Neither distillation *in vacuo* nor column chromatography proved suitable for the purification of *S,N*-ketene acetals **1**, because of considerable decomposition. Therefore, a synthetic procedure was developed by which *S,N*-ketene acetals of good purity could be obtained from the reaction mixture by means of extraction only. A small excess of lithiated phosphine oxide **2a-c** was used, so as to achieve complete conversion of the aldehyde. Lithium diphenylphosphinate (**6**), which is the side product of the Horner-Wittig reaction, was easily removed by extraction with water. Finally, any remaining **2a-c** was separated from the *S,N*-ketene acetal by trituration with petroleum ether (40/60). Evaporation of the solvent *in vacuo* afforded *S,N*-ketene acetals **1a-j**, derived from aromatic aldehydes, in excellent yields (Table 2). The purity was better than 95%, as could be judged from ^{1}H- and ^{13}C-NMR. *S,N*-ketene acetals **1b-j** are new compounds.

Table 2. Synthesis of *S,N*-ketene Acetals **1a-j**

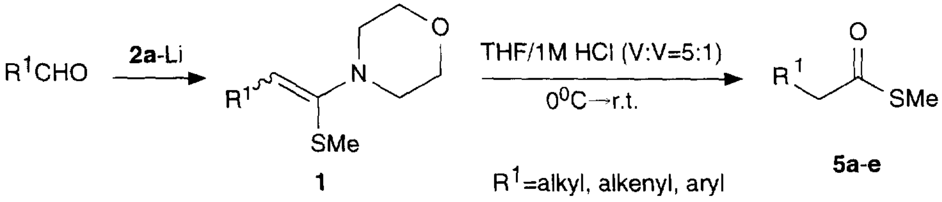
Compound	R^1	R^2	X	Yield (%)
1a	phenyl	methyl	O	90
1b	phenyl	*n*-butyl	O	88
1c	phenyl	methyl	CH_2	80
1d	*p*-methoxyphenyl	methyl	O	88
1e	*p*-methoxyphenyl	*n*-butyl	O	81
1f	*p*-methoxyphenyl	methyl	CH_2	80
1g	2-thienyl	methyl	O	80
1h	2-thienyl	*n*-butyl	O	84
1i	*m*-bromophenyl	methyl	O	89
1j	*m*-bromophenyl	methyl	CH_2	85

S,N-ketene acetals **1a-j** were isolated as mixtures containing approximately equal amounts of the *E*- and *Z*-isomers. Traces of acid, such as often present in $CDCl_3$, catalyzed a rapid isomerization of the double bond. This facilitated discrimination between the ^{1}H- and ^{13}C-NMR signals of the *E*- and *Z*-isomers. It is believed that isomerization of **1a-j** will lead to a predominance of the *Z*-isomer, as a result of greater steric congestion between the aromatic ring and the amino substituent in the *E*-isomer[10]. The *Z*-configuration was confirmed by the observation of *NOE*-effects between the vinylic proton and the NCH_2-groups in the major isomer of compounds **1g** and **1i**, after isomerization had occurred. Therefore, it is assumed that in all *S,N*-ketene acetals **1a-j**, the *Z*-isomer is the thermodynamically more stable one. The *Z*:*E*-ratios observed for compounds **1a-j** after equilibration varied between 2:1 and 3:1. *S,N*-ketene acetal **1h**, which carries the smaller 2-thienyl substituent at the ß-carbon atom, showed no signs of isomerization. Schuijl *et al.* assigned the low field ^{1}H-NMR signal in the vinylic region of *S,N*-ketene acetals to the

Z-isomer[7a]. We found the chemical shift of the vinylic protons of **1a-j** to be an unreliable indicator for assignment of the *E*- and Z-configuration [Compare, *e.g.*, compounds **1g** (δ: 6.06 ppm (*Z*)-CH=; 6.22 ppm (*E*)-CH=) and **1i** (δ: 5.66 ppm (*Z*)-CH=; 5.59 ppm (*E*)-CH=]. The ^{1}H-NMR signal of the SCH_3 or SCH_2 groups of the Z-isomers, on the other hand, appeared at higher field than those of the *E*-isomers in all cases studied here. This signal therefore appears to be a more reliable indicator for configurational assignment. Selected ^{1}H- and ^{13}C-NMR data of compounds **1a-j** are presented in the experimental part.

The procedure described above gave pure *S,N*-ketene acetals only in the case of aldehydes which possess no α-hydrogen atoms, *i.e.* aromatic aldehydes. The use of aliphatic aldehydes resulted in the isolation of slightly contaminated *S,N*-ketene acetals **1**, R^1=alkyl. These contaminations probably resulted from aldol condensation of the aldehydes used, promoted by the basic phosphine oxide anions **2a-c**-Li. As the *S,N*-ketene acetals **1** do not withstand the conditions of column chromatography, these impurities could not be removed. It turned out, however, that the *S,N*-ketene acetals **1** could be easily transformed into more stable (*S*)-thioesters **5**.

Acid-catalyzed Hydrolysis of S,N-ketene Acetals. Conversion of Aldehydes to Homologous (S)-thioesters Treatment of *S,N*-ketene acetal **1a** with aqueous hydrochloric acid at room temperature (eq. 3) resulted in its selective hydrolysis to (*S*-Me)-thioester **5a**, R^1=Ph which was obtained in 81% yield, calculated on benzaldehyde. Starting from 2-thiophenecarboxaldehyde, thioester **5b**, R^1=2-thienyl was similarly prepared in a yield of 57%.



(*3*)

Table 3. (*S*-Me)-thioesters **5a-e**

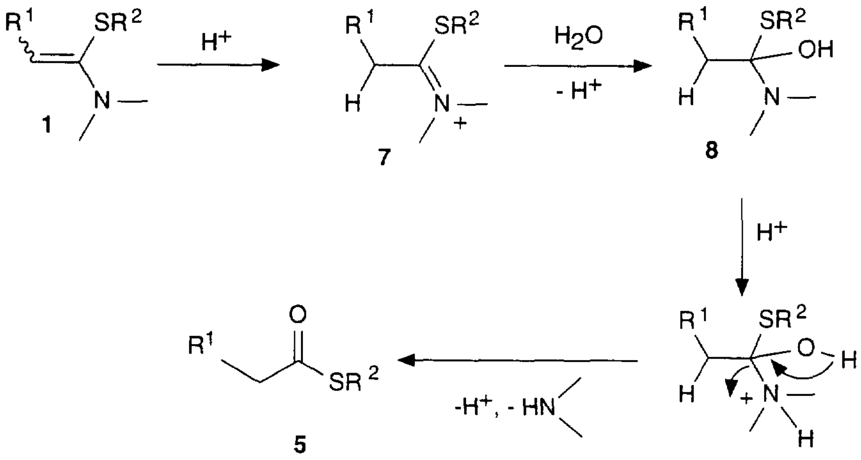
Compound	R^1	Yield (%)[a]
5a	phenyl	81
5b	2-thienyl	57
5c	*c*-hexyl	73
5d	2-phenylethyl	70
5e	(*E*)-2-phenylethenyl	74

[a] Based on aldehyde R^1CHO.

The selective hydrolysis of *S,N*-ketene acetals **1** to (*S*)-thioesters **5**, allowed better use of the Horner-Wittig reaction of lithiated phosphine oxide **2a** with aliphatic aldehydes. Thus, cyclohexanecarboxaldehyde and 3-phenylpropionaldehyde were converted to (*S*)-thioesters **5c** and **5d** in good overall yields by a Horner-Wittig reaction with **3a**-Li, followed by hydrolysis of the crude *S,N*-ketene acetal (Table 3).

Starting from cinnamaldehyde, unsaturated thioester **5e** was similarly prepared in a yield of 74%. The downfield position of the carbonyl atom resonance at 197.5 ppm in the ^{13}C-NMR spectrum suggested **5e** to be a β,γ-unsaturated thioester. This was confirmed by IR-spectroscopy: the C=O groups of thioester **5e** and saturated thioester **5c** both absorb at 1790 cm^{-1}. Apparently, upon acid-catalyzed hydrolysis of *S,N*-ketene acetal **1**, $R^1 = CH_2{=}CHPh$, the β-carbon atom of the dienyl skeleton is preferentially protonated, leading to formation of the β,γ-unsaturated thioester. Under the mildly acidic conditions used, no double bond isomerization takes place. The double bond of **5e** has a *trans*-configuration, as was deduced from the coupling constant between the vinylic protons ($J_{H\beta\text{-}H\gamma}$=15.5 Hz). Thioesters **5b**, **5c** and **5e** are new compounds[11a,b].

A likely mechanism for this hydrolysis, which closely resembles the mechanism of the hydrolysis of enamines under acidic conditions[12], is depicted in Scheme 2.



Scheme 2.

It is assumed that the hydrolysis starts with protonation at the electron rich β-carbon atom of the *S,N*-ketene acetal, leading to formation of iminium intermediate **7**. Attack of a molecule of water at the iminium carbon atom of **7**, followed by loss of a proton, then leads to formation of poly-hetero-substituted intermediate **8**. Protonation at nitrogen in **8** initiates elimination of the secondary amine and formation of thioester **5**. The hydrolysis showed excellent chemoselectivity. Protonation at sulfur in **8**, followed by loss of methanethiol, would have given the corresponding amide. Yet, under the present reaction conditions (THF/1M HCl, V:V=5:1, r.t.), no amide formation was observed. Apparently, the difference in basicity between nitrogen and sulfur is large enough to cause the observed highly selective course of the hydrolysis reaction.

Concluding Remarks

S,N-ketene acetals **1** are accessible in high yields by the Horner-Wittig reaction. The requisite *S,N*-acetals of formyldiphenylphosphine oxide **2a-c**, are readily obtained in good yields by aminolysis of [(α-chloro)-thiomethyl]diphenylphosphine oxides **3a** and **3b**. The lithiated phosphine oxides **2a-c** are stable in solution, even at room temperature, and react efficiently with several structural types of aldehydes. When subjected to hydrolysis under mildly acidic conditions, *S,N*-ketene acetals **1** are quantitatively converted into (*S*)-thioesters **5**. This easy and hitherto undescribed hydrolysis of *S,N*-ketene acetals provided the basis for a simple and efficient two-step procedure for the conversion of aldehydes to their one-carbon-homologated (*S*)-thioesters.

EXPERIMENTAL

THF (from $LiAlH_4$), CH_2Cl_2 (from CaH_2), EtOAc and petroleum ether (40/60) were distilled before use. Column chromatography was performed using Merck Kieselgel 60 (0.0040-0.0063 mm). TLC analyses were performed on Schleicher and Schuell F1500/LS 254 silica plates, using UV detection or a spray of $KMnO_4$ in acetone. ^{1}H- (200 MHz), ^{13}C- (50 MHz) and ^{31}P- (80 MHz) NMR spectra were recorded on a Jeol NM FX-200 spectrometer using deuterochloroform. Chemical shifts are given in ppm (δ) relative to internal tetramethylsilane (^{1}H-NMR), internal deuterochloroform (^{13}C-NMR) or external 85% phosphoric acid (^{31}P-NMR). Coupling constants (J) are given in Hz. IR-spectra were recorded on a Pye Unicam SP3-200 spectrometer. Melting points were determined on a Büchi melting point apparatus and are uncorrected. Elemental analyses were performed at the Microanalytical Laboratory, Department of Chemistry, University College Dublin, Ireland.

4-[(Diphenylphosphinoyl)(methylthio)methyl]morpholine (**2a**). A 250 ml round-bottomed flask was charged with 120 ml of freshly distilled morpholine and 11.07 g (38.6 mmol) of phosphine oxide **3a** in a nitrogen atmosphere. The suspension was slowly heated to 80°C. The phosphine oxide gradually dissolved. After a few minutes, a white solid started to precipitate. The reaction mixture was maintained at 80°C for 1 h. The resulting white suspension was allowed to cool to room temperature and poured into 300 ml of demineralized water. After stirring for 0.5 h, the aqueous suspension was filtered over a Büchner funnel. The solid residue was washed twice with 100 ml of demineralized water and dissolved in 200 ml of CH_2Cl_2. This solution was extracted once with 100 ml of saturated K_2CO_3, twice with demineralized water and dried overnight with $MgSO_4/K_2CO_3$. The solvent was evaporated *in vacuo*, leaving a white solid which was crystallized from CH_2Cl_2/petroleum ether (40/60) to give 9.29 g (27 mmol, 70%) of phosphine oxide **2a**. ^{1}H-NMR: δ 2.05 (s, 3H, SCH_3); 2.52-2.68 (m, 2H, NCH_2); 3.04-3.20 (m, 2H, NCH_2); 3.40-3.64 (m, 4H, CH_2O); 4.36 (d, J_{PH}=8.7, 1H, P-CH); 7.40-7.60 (m, 6H); 7.76-8.00 (m, 4H). ^{13}C-NMR: δ 18.5 (SCH_3); 50.4 (NCH_2); 66.5 (CH_2O); 75.1 (d, J_{PC}=92, P-C). ^{31}P-NMR: δ 30.0. M.p. 146-8°C [lit[6]. M.p. 145-7°C].

4-[(n-Butylthio)(diphenylphosphinoyl)methyl]morpholine (**2b**). Phosphine oxide **2b** was similarly obtained from **3b** in 69% yield after a crystallization from EtOAc. ^{1}H-NMR: δ 0.74 (t, J=7.3, 3H, CH_3); 1.04-1.36 (m, 4H, $(CH_2)_2$); 2.08-2.36 (m, 2H, SCH_2); 2.40-2.64 (m, 2H, NCH_2); 2.52-2.72 (m, 1H, NCH_2); 2.96-3.16 (m, 1H, NCH_2); 3.40-3.68 (m, 4H, CH_2O); 4.40 (d, J_{PH}=8.7, 1H, P-CH); 7.32-7.60 (m, 6H); 7.68-8.00 (m, 4H). ^{13}C-NMR: δ 13.5 (CH_3); 21.5 (CH_2); 31.8, 35.0 (SCH_2, CH_2); 50.4 (NCH_2); 66.6 (CH_2O); 74.2 (d, J_{PC}=92, P-C). ^{31}P-NMR: δ 29.8. Anal. cald. for $C_{21}H_{28}NO_2PS$ (389.49): C 64.76 H 7.25 N 3.59; found: C 64.94 H 7.25 N 3.42. M.p. 166-8°C.

1-[(Diphenylphosphinoyl)(methylthio)methyl]piperidine (**2c**). Phosphine oxide **2c** was similarly obtained from **3a** in 72 % yield after a crystallization from CH_2Cl_2/petroleum ether (40/60). ^{1}H-NMR: δ 1.20-1.60

(m, 6H, $(CH_2)_3$); 2.03 (s, 3H, SCH_3); 2.44-2.68 (m, 2H, NCH_2); 2.92-3.06 (m, 2H, NCH_2); 4.41 (d, J_{PH}=9.3, 1H, P-CH); 7.32-7.60 (m, 6H); 7.76-8.00 (m, 4H). ^{13}C-NMR: δ 19.3 (SCH_3); 24.1 (CH_2); 26.3 (CH_2); 52.2 (NCH_2); 77.4 (d, J_{PC}=94, P-C). ^{31}P-NMR: δ 29.4. Anal. cald. for $C_{19}H_{24}NOPS$: C 66.06 H 7.00 N 4.05; found: C 65.58 H 6.94 N 3.90. M.p. 192-5°C.

General procedure for the synthesis of S,N-ketene acetals 1a-j. In an atmosphere of dry nitrogen, lithium-*di*-isopropylamide (4.4 mmol, freshly prepared from *di*-isopropylamine (0.7 ml, 5 mmol) and 2.75 ml of a 1.6 M solution of *n*-BuLi in hexanes (4.4 mmol) in 10 ml of dry THF at 0°C) was added to a suspension of 4 mmol of phosphine oxide **2a-c** in 40 ml of dry THF at -10°C. After stirring for 30 min at this temperature, the neat aldehyde (3.6 mmol) was added in one portion to the yellow solution. This resulted in an exothermic reaction and the instantaneous formation of a white precipitate. The reaction mixture was allowed to warm to room temperature and stirring was continued for 1 h. The resulting yellow suspension was poured into a mixture of 100 ml of demineralized water and 150 ml of petroleum ether (40/60), followed by extraction and separation of the layers. The organic layer was extracted once with 100 ml of demineralized water and dried with $MgSO_4$. The solvent was evaporated *in vacuo* at room temperature. The obtained white mass was triturated with 10 ml of petroleum ether (40/60) and filtered. The solvent was evaporated *in vacuo* at room temperature to give *S,N*-ketene acetals **1a-j** of high purity as colorless liquids. Selected ^{1}H- and ^{13}C-NMR data of compounds **1a-j** are presented in Table 4.

Table 4. ^{1}H- and ^{13}C-NMR Data of *S,N*-ketene Acetals **1a-j**

Compound	δ(CH=) (ppm)	δ(SCH) (ppm)	δ(HC=) (ppm)	δ(=C) (ppm)
	E, *Z*	*E*, *Z*	*E*, *Z*	*E*, *Z*
1a	5.75, 5.79	2.32, 2.16	111.9, 111.1	148.9, 147.7
1b	5.89, 5.83	2.72, 2.60	114.0, 112.4	147.0, 146.6
1c	5.69, 5.72	2.30, 2.15	110.4, 110.3	150.1, 148.9
1d	5.77[a]	2.31, 2.15	113.5, 111.1	146.7, 146.3
1e	5.91, 5.80	2.70, 2.60	115.6, 113.2	144.7, 145.0
1f	5.70[a]	2.28, 2.14	110.1, 111.9	148.0, 147.4
1g	6.22. 6.06	2.36, 2.25	114.1, 106.6	146.9, 145.1
1h[b]	6.11, 6.35	2.79, 2.71	117.1, 107.9	145.2, 144.0
1i	5.59, 5.66	2.32, 2.17	109.1[a]	150.9, 148.9
1j	5.53, 5.59	2.29, 2.16	107.8, 108.2	152.1, 150.9

[a] Coinciding signals. [b] *E*:*Z* = 1:1.

General Procedure for the Synthesis of (S)-thioesters 5a-e. The intermediate *S,N*-ketene acetal **1**, obtained as described above, was dissolved in 50 ml of THF. At 0°C, 10 ml of a 1M HCl solution was added. The reaction mixture was allowed to warm to room temperature and stirring was continued for 1h. The reaction mixture was poured into 100 ml of demineralized water and extracted three times with 50 ml of petroleum ether (40/60). The combined organic layers were extracted three times with 50 ml of demineralized water, dried with $\mathrm{MgSO_4}$ and the solvent was evaporated *in vacuo*. The crude thioester was purified by column chromatography (eluent: petroleum ether (40/60), diethyl ether).

(S)-Methyl (2-thienyl)ethanethioate (**5b**). ^{1}H-NMR: δ 2.31 (s, 3H, $\mathrm{SCH_3}$); 4.03 (s, 2H, $\mathrm{CH_2}$); 6.92-7.04 (m, 2H); 7.20-7.28 (m, 1H). ^{13}C-NMR: δ 11.7 ($\mathrm{SCH_3}$); 43.7 ($\mathrm{CH_2}$); 125.3, 126.8, 127.3 (CH); 134.4 (*ipso*-C); 196.5 (C=O). Anal. cald. for $\mathrm{C_7H_8OS_2}$ (172.25): C 48.77 H 4.68; found: C 47.62 H 4.63.

(S)-Methyl (cyclohexyl)ethanethioate (**5c**). ^{1}H-NMR: δ 0.86-1.36 (m, 6H, $\mathrm{CH_2}$); 1.48-1.76 (m, 4H, $\mathrm{CH_2}$); 1.76-1.98 (m, 1H, CH); 2.29 (s, 3H, $\mathrm{SCH_3}$); 2.43 (d, 2H, J=6.7, $\mathrm{CH_2C{=}O}$). ^{13}C-NMR: δ 11.4 ($\mathrm{SCH_3}$); 25.8, 26.0, 35.5 ($\mathrm{CH_2}$); 51.3 (CH); 198.9 (C=O). Anal. cald. for $\mathrm{C_9H_{16}OS}$ (172.28): C 62.69 H 9.36; found: C 62.67 H 9.04.

(S)-Methyl 4-phenylbutanethioate (**5d**). ^{1}H-NMR: δ 2.00 (q, J=7, 2H, $\mathrm{CH_2}$); 2.30 (s, 3H, $\mathrm{SCH_3}$); 2.58 (t, J=7.2, 2H) and 2.66 (t, J=7.7, 2H, $\mathrm{CH_2}$-Ph and $\mathrm{CH_2}$-C=O). ^{13}C-NMR: δ 11.2 ($\mathrm{SCH_3}$); 26.9, 34.6, 42.8 ($\mathrm{(CH_2)_3}$); 125.8, 128.1, 128.2 (CH); 140.9 (*ipso*-C); 199.0 (C=O).

(S)-Methyl (E)-4-phenyl-3-butenethioate (**5e**). ^{1}H-NMR: δ 2.31 (s, 3H, $\mathrm{SCH_3}$); 3.45 (d, 2H, J=7.2, $\mathrm{CH_2}$); 6.16-6.36 (m, 1H, =CH); 6.54 (d, 1H, J=15.5, =CH); 7.16-7.40 (m, 5H). ^{13}C-NMR: δ 11.5 ($\mathrm{SCH_3}$); 47.4 ($\mathrm{CH_2}$); 121.0 (=CHC(=O)); 126.2, 127.5, 128.4 (CH); 134.5 ($\mathrm{CH_2CH{=}}$); 136.5 (*ipso*-C); 197.5 (C=O). Anal. cald. for $\mathrm{C_{11}H_{12}OS}$ (192.28): C 68.65 H 6.29; found: C 67.44 H 6.34.

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