Tetrahedron 64 (2008) 11865–11875

Contents lists available at ScienceDirect

Tetrahedron

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

Intramolecular homolytic substitution at the sulfur atom: an alternative way to generate phosphorus- and sulfur-centered radicals

Paola Carta, Nicolas Puljic, Carine Robert, Anne-Lise Dhimane, Cyril Ollivier, Louis Fensterbank *, Emmanuel Lacôte *, Max Malacria *

UPMC Univ Paris 06, Laboratoire de Chimie Organique (UMR CNRS 7611), Institut de chimie moléculaire (FR 2769), 4 place Jussieu, C. 229, 75005 Paris, France

ARTICLE INFO

Article history:
Received 15 July 2008
Accepted 29 August 2008
Available online 20 September 2008

ABSTRACT

Two efficient procedures involving tin hydride or thiophenol-mediated intramolecular homolytic substitution at the sulfur atom are reported. They lead to the generation of varied *P*(V)-centered radicals from the corresponding aryl or alkyne thiophosphorus substrates. The radical formed can be trapped by an olefin via an intermolecular addition, leading to the construction of C–P bonds. Thiophosphination of triple bonds was also achieved using a radical cycloisomerization process. Extension of the methodology to sulfur-containing species was examined.

1. Introduction

The discovery of new, mild, and reliable methods for the construction of carbon–heteroatom bonds is still an essential objective for today's organic chemists.[1] Indeed, heteroatoms are first-rate assets to modulate the properties of matter and/or to lead to molecular recognition. Nature has made abundant use of this opportunity. Thus, the periodic table offers significant opportunities to go beyond naturally occurring structures and chemical functions. But heavier elements have unique properties that are still not fully explored and that one needs to master in order to devise efficient methodologies leading to new motifs.

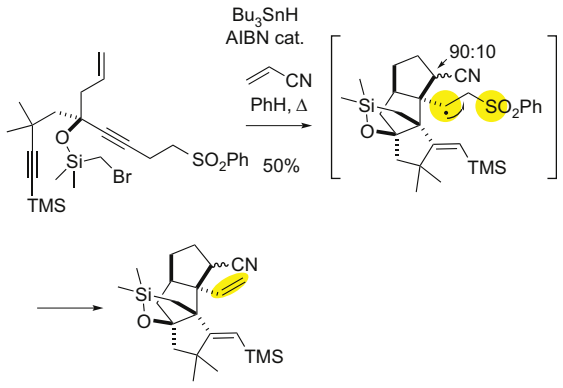
For the last decade, we have been involved in designing new radical processes in which heteroatom-centered radicals play a key-role. This has led us to investigate homolytic substitutions to construct C–P bonds.[2] In this article, we wish to give a full account of this work, including an overview of its genesis.

1.1. Background of the present work

Following Julia's,[3] Stork's,[4] and Curran's[5] seminal contributions to radical cascades, our group has been originally attracted by the great potential those bio-inspired processes offer to organic synthesis.[6] We wished to use Nature's lead to control reactivity toward one pot assembly of enantiopure complex molecules from simple, acyclic, achiral building-blocks.

Among the challenges we have faced to avoid the generation of mixtures of compounds, three issues were especially trying. Design of a successful asymmetric process requires a subtle yet strong master plan, an efficient termination, and a source of chiral information.

Tuning the different features of radical reactions allowed us to introduce reactions previously considered to be forbidden (or very rare), such as the 5-*endo*-*trig*[7] and 4-*exo*-*dig*[8] radical cyclizations, and the 1,4-H translocation.[9] Our take on the two other issues led us to consider heteroatom-based processes. For example, β-elimination of a sulfonyl radical led to the triquinane framework in high yields, a process that introduced five C–C bonds and five stereogenic elements— including four quaternary carbons—in one single step (Scheme 1).[10] On the other hand, chiral sulfoxides were our entry point into asymmetric radical synthesis.[11]

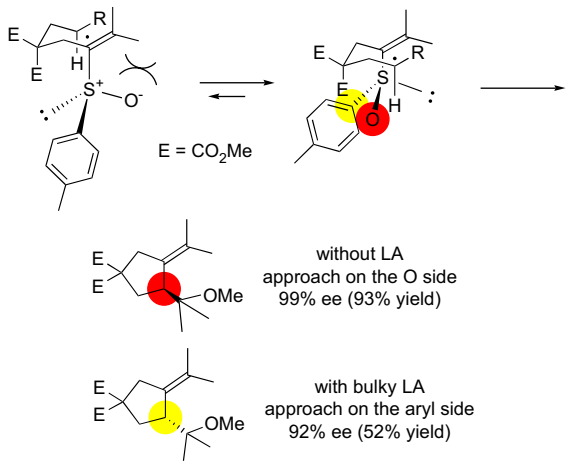


Scheme 1. Radical cascade leading to linear triquinanes.

* Corresponding authors. Tel.: +33 1 44 27 70 68; fax: +33 1 44 27 73 60 (L.F.); tel.: +33 1 44 27 25 47; fax: +33 1 44 27 73 60 (E.L.); tel.: +33 1 44 27 35 86; fax: +33 1 44 27 73 60 (M.M.).
E-mail addresses: louis.fensterbank@upmc.fr (L. Fensterbank), emmanuel.lacote@upmc.fr (E. Lacôte), max.malacria@upmc.fr (M. Malacria).

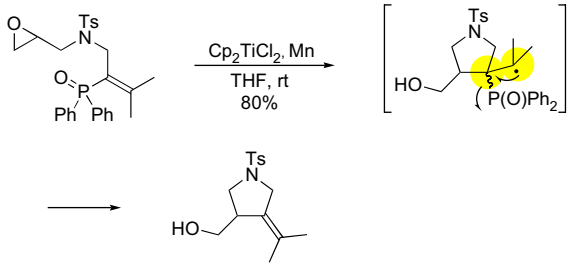
0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.08.108

This led us to craft a domino process using the sulfinyl moiety as both chiral auxiliary and terminating trigger. In the process, we devised an asymmetric intramolecular vinylation of prochiral radicals (Scheme 2). Coordination of Lewis acids to the sulfoxide led to a complete reversal of the stereochemical outcome of the vinylation.[12] This work was part of a coordinated effort with the Renaud group, who tailored a variation on that concept in which the sulfoxide led to desymmetrization during a 1,5-H transfer followed by the same β-sulfinyl radical elimination.[13]



Scheme 2. Asymmetric intramolecular vinylation of prochiral radicals.

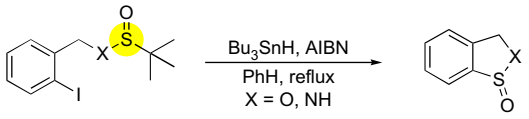
We next tried to extend the scope of the sulfinyl induction to the 5-*endo*-*trig* process, which led us to the accidental discovery of the first elimination of a *P*(V)-centered radical, a process formerly thought impossible.[14] We have examined this interesting reaction more in-depth, and applied it to radical vinylations (Scheme 3).[15] Others have since introduced related P˙ β-eliminations for allylations,[16] carbonylations,[17] or arylations.[18]



Scheme 3. Radical vinylation via P˙β-elimination.

Our foray into the chemistry of *S*- and *P*-centered radicals led us to consider homolytic substitutions as a promising territory to uncover valuable new reactions. The former are highly versatile because they can be used both to create selected bonds, or to generate particular radicals.[19]

Facile extrusion of a cheap *tert*-butyl radical from sulfinates and sulfinamides delivered interesting sulfur-containing heterocycles (Scheme 4).[20] To date, this is the highest oxidation state at sulfur compatible with the homolytic substitution mechanism. Conversely, homolytic substitution at the sulfur atom in thiophosphorus compounds led us to devise a new way to generate phosphorus-centered radicals, which formed the basis of a recent communication from our group.[2] We report herein the full scope of this method.



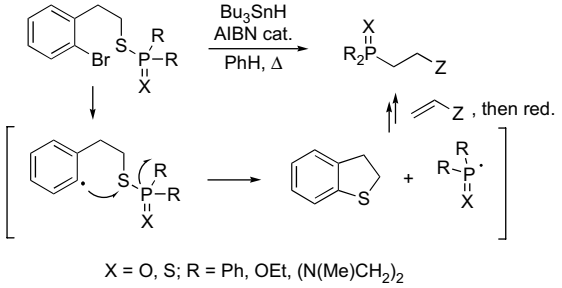
Scheme 4. Homolytic substitution at oxidized sulfur.

2. Construction of carbon–phosphorus bonds

2.1. Tin hydride-mediated homolytic substitution at sulfur/phosphorus-centered radicals addition tandem reaction

Generation of a wide range of phosphorus-centered radicals has generally relied on homolytic cleavage of P–X bonds (X=Se, S, P), or hydrogen abstraction from P–H systems.[21–23] We reasoned that intramolecular homolytic substitution at sulfur might be an interesting alternative to access the target intermediates.[19c]

In 1996, Crich showed that tin-mediated aryl radical cyclizations onto thioesters derived from (iodoaryl)-thiols led to the formation of acyl radicals.[24] Taking inspiration from this approach, we decided to examine the behavior of thiosphononate analogues **1a–c** toward generating *P*(V)-centered radicals. Evidence for formation of the latter was sought from intramolecular trapping experiments with alkenes (Scheme 5).



Scheme 5. Generation of *P*-centered radicals via intramolecular homolytic substitution.

2.2. Synthesis of the substrates

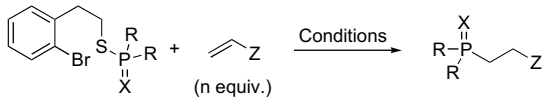
Radical thiophosphonate precursors **1a–c** were prepared in moderate to good yields from sodium 2-(2′-bromophenyl)ethanethiolate by nucleophilic substitution of the corresponding chlorophosphonate reagent. The starting thiol was obtained following a known procedure,[24a] or a modified one (see Section 5).

2.3. Scope of the homolytic substitution/*P*-centered radicals' radical addition tandem reaction

We examined the reactivity of thiophosphonates **1a–c**. These compounds were submitted to two different sets of conditions. Method A involved standard syringe pump addition of tributyltin hydride (TBTH) in the presence of AIBN and an olefin in refluxing benzene. Method B is adapted from Stork's catalytic conditions ((Bu$_3$SnCl, 12 mol %), NaBH$_4$, and the olefin in refluxing *t*-BuOH). We selected an array of electronically different olefins (electron-poor, -rich, and neutral) to get more data on the reactivity of the phosphorus-centered radical (Table 1).

When employing Method A, substrates **1a–c** efficiently led to phosphinoyl, phosphonyl, and diaminophosphonyl radicals, which added onto alkenes in moderate to good yields. Reactivity depended on the nature of the radical formed, as well as that of the olefin. In a typical experiment, phosphine oxide **2a** was formed in 84% from **1a** and 1-octene (Table 1, entry 1). 1-Octene (10 equiv) was

Table 1



1a X = O, R = Ph
1b X = O, R = OEt
1c X = O, R = $(N(Me)CH_2)_2$

2a-c, Z = *n*-Hex
3a-c, Z = CN
4a-c, Z = O-*t*Bu

Entry	1	Z	*n*	Condition	2–4[a]	Yield (%)
1	**1a**	*n*-Hex	10	A	**2a**	84
2	**1a**	*n*-Hex	2	B	**2a**	58
3	**1a**	CN	2	A	**3a**	39
4	**1a**	CN	2	B	**3a**	50
5	**1a**	O-*t*-Bu	10	A	**4a**	71[b]
6	**1a**	O-*t*-Bu	10	B	**4a**	47[c]
7	**1b**	*n*-Hex	10	A	**2b**	75
8	**1b**	*n*-Hex	10	B	**2b**	70
9	**1b**	CN	10	A	**3b**	74[d]
10	**1b**	O-*t*-Bu	10	B	**4b**	56
11	**1c**	*n*-Hex	10	A	**2c**	62[e]
12	**1c**	*n*-Hex	10	B	**2c**	48
13	**1c**	CN	2	A	**3c**	82
15	**1c**	O-*t*-Bu	10	A	**4c**	40[f]

[a] Method A: Bu_3SnH (1.2 equiv) AIBN (0.25 equiv), slow addition (0.2 mmol h^{-1}), PhH, reflux. Method B: Bu_3SnCl (12 mol %), $NaBH_4$, *t*-BuOH, reflux.
[b] Adduct was contaminated by approx. 20% of an unknown by-product.
[c] Adduct was contaminated by approx. 10% of an unknown by-product.
[d] Approx. 50% of oligomers.
[e] Reduced S.M. (10–30%) was also observed.
[f] Product is not stable.

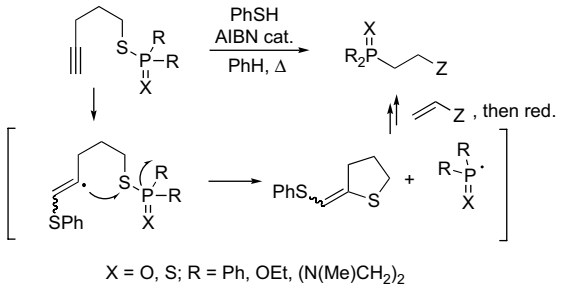
necessary to reach optimal yield. Phosphinoyl radicals are indeed believed to be predominantly nucleophilic.[21] Our results seem to contradict this, since diphenylphosphinoyl radical addition gave better yields with enol ethers than with acrylonitrile (compare entries 3 and 5). However, this reading is skewed due to polymerization of acrylonitrile. Indeed, we performed competition experiments between acrylonitrile and *tert*-butyl vinyl ether, and only isolated **3a** in 28% yield, which tends to confirm that phosphinoyl radicals were predominantly nucleophilic.

The reaction proved quite general. Thiophosphonate **1b** generated phosphonyl radical leading to the corresponding adducts **2b**–**4b** in good yields (Table 1, entries 7, 9, and 10). Diaminophosphonyl radicals were investigated next. These intermediates had been overlooked in the radical literature. We were pleased to observe addition products from substrate **1c**. Diaminophosphonates **2c**–**4c** were isolated after standard purification but proved unstable to even short term storage. Method B was in most cases less efficient, as the adducts were isolated in slightly lower yields.

2.4. Tin-free conditions: thiophenol as mediator

The Benati/Spagnolo group developed a tin-free methodology to generate alkyl and acyl radicals.[25] It relies on addition of the benzenesulfanyl radical to the triple bond of alkyl or acyl 4-pentynyl sulfides followed by homolytic substitution of the resulting transient β-(phenylsulfanyl)vinyl radicals at the sulfur atom, leading to the formation of the desired radical. We thus decided to extend the scope of this procedure to the generation of *P*(V)-centered radicals (Scheme 6).

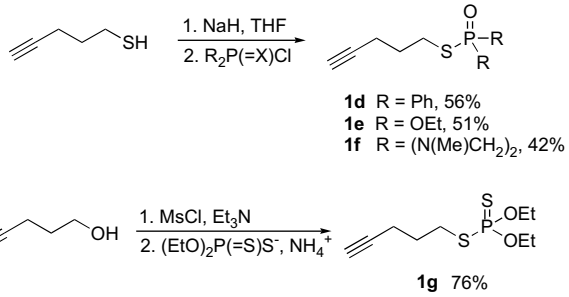
Again, *S*-pentynyl thiophosphonates **1d**–**f** were easily prepared from pent-4-yne-1-thiol and the corresponding chlorophosphonate reagent, as previously reported for thiophosphonates **1a**–**c** (Scheme 7). Pent-4-yne-1-thiol was obtained by nucleophilic displacement with cesium thioacetate followed by saponification of the intermediate thioacetate. *S*-Pentynyl thiophosphonate **1g** was readily



X = O, S; R = Ph, OEt, $(N(Me)CH_2)_2$

Scheme 6. Thiophenol-mediated generation of phosphorus-centered radicals.

synthesized from nucleophilic substitution of the mesylate of pentynol with the ammonium salt of *O*,*O*-diethyl thiophosphate. The reaction required strictly degassed DMF and an inert atmosphere to avoid oxidation of the P═S bond to **1e**.



1d R = Ph, 56%
1e R = OEt, 51%
1f R = $(N(Me)CH_2)_2$, 42%

1g 76%

Scheme 7. Preparation of **1d**–**g**.

The substrates were refluxed in toluene in the presence of PhSH, various alkenes, and slowly added AIBN (0.15 mmol h^{-1}). Compound **1d** proved to be an excellent precursor of phosphine oxide adducts. Surprisingly, access to phosphonates following this protocol was poorly efficient, while diaminophosphonyl compounds could not be isolated pure. The methodology was then extended to the thiophosphonates, such as **1g**, which proved to be an excellent precursor of diethoxy phosphonothioyl radicals. 2-(Phenylthiomethylene) tetrahydrothiophene[25] was isolated in all cases as a by-product (Table 2).

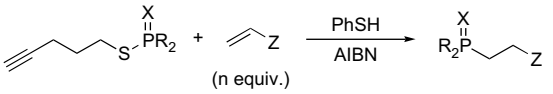
Smooth addition to 1-octene occurred, while the other alkenes reacted only moderately. Hydrothiolated by-products (thiophenol addition with no cyclization) were also isolated in variable amounts, depending on the nature of the starting substrate. Finally, it is worthy of note that *S*-pentenyl thiophosphonate **1h**, with an alkene in lieu of the alkyne did not react under our conditions. This lack of reactivity can be attributed either to the lowered bond energy of an alkyl sp^3 C–S bond relative to that of a sp^2 C–S bond, or to a greater reversibility of the addition step. Both properties are expected to diminish the efficiency of the homolytic substitutions.

3. Bis-heterofunctionalization of unsaturations

3.1. Thiophosphorylation of triple bonds involving a cycloisomerization reaction

P-Centered radicals are known to add to alkynes.[23i] We reasoned that the absence of alkene in the previous reaction would guide the generated radicals toward addition onto the triple bond thus leading to a cycloisomerization of the starting material, which amounts to hetero bis-functionalization of alkynes (Scheme 8).

Table 2

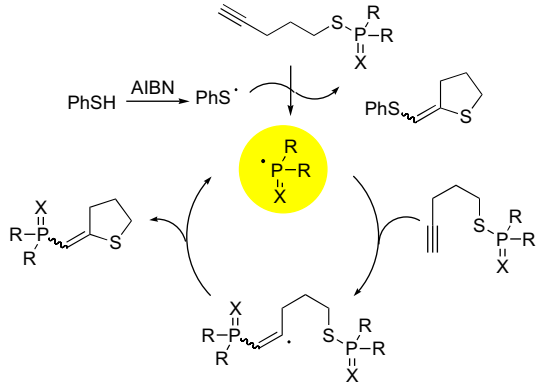


1d X = O,R = Ph
1e X = O, R = OEt
1f X = O,R = $(N(Me)CH_2)_2$
1g X = S, R = OEt

2a-c, Z = *n*-Hex, X = O
2d, Z = *n*-Hex, X = S
3a-c, Z = CN, X = O
3d, Z = CN, X = S
4a-c, Z = O-*t*Bu, X = O
4d, Z = O-*t*Bu, X = S

Entry	1	Z	*n*	2–4[a]	Yield (%)
1	**1d**	*n*-Hex	10	**2a**	87
2	**1d**	*n*-Hex	2	**2a**	57
3	**1d**	CN	2	**3a**	66[b]
4	**1d**	O-*t*-Bu	5	**4a**	63[c]
5	**1e**	*n*-Hex	10	**2b**	58[d]
7	**1e**	*n*-Hex	2	**2b**	29[e]
8	**1f**	*n*-Hex	10	**2c**	~40[f]
9	**1f**	CN	4	**3c**	~20[f]
10	**1f**	O-*t*-Bu	5	**4c**	~40[f]
11	**1g**	*n*-Hex	10	**2d**	93
12	**1g**	CN	5	**3d**	48
15	**1g**	O-*t*-Bu	5	**4d**	61

[a] Method C: PhSH (1.1 equiv), AIBN (0.2 equiv), slow addition (0.15 mmol h^{-1}), Tol. reflux.
[b] Product was contaminated by approx. 30% of an undefined by-product.
[c] Product was contaminated by approx. 40% of $Ph_2P(O)CH_2CHO$, a by-product resulting from oxidation of the transient radical formed after addition.
[d] Hydrothiolation adducts (28%) were also isolated.
[e] Hydrothiolation adducts (23%) were also isolated.
[f] Yields are estimated based on the NMR ratios. Products were contaminated by unknown phosphorus-containing by-products.



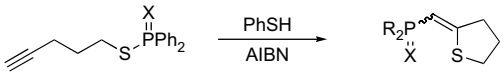
Scheme 8. Mechanism of the proposed cycloisomerization.

Such concomitant thiophosphorylations of both ends of an alkyne are quite rare[26] and, to the best of our knowledge, ours was the first example of such a process in radical chemistry. Thiophenol was only required to trigger formation of the initial *P*-centered radicals, thus only a substoichiometric amount of mediator was needed (Table 3).

In the absence of alkene and under the previously described reaction conditions, *S*-pentynyl thiophosphine oxide **1d**, as well as *S*-pentynyl dithiophosphonate **1g**, underwent a clean cycloisomerization. Heterocycle **5a** (respectively, **5d**) was isolated in good yield as a 70:30 (respectively, 50:50) mixture of *Z*/*E* isomers. Assignment of the stereochemistry was determined by NOE.

Optimal conditions were found with 0.4 equiv of thiophenol (Table 3). Replacement of toluene by *tert*-butanol was detrimental to the reactivity. The cycloisomerizations of diethoxy- and diaminophosphonate derivatives **1e** and **1f** proceeded sluggishly and only traces of the expected adducts were observed. This appears to match the behavior of the same substrates in the previous reaction. We have no clear explanation to account for this reactivity difference. Moreover, the process could not be extended to the formation of other ring sizes.

Table 3



1d X = O, R = Ph
1e X = O, R = OEt
1f X = O, R = $(N(Me)CH_2)_2$
1g X = S, R = OEt

5a X = O, R = Ph
5b X = O, R = OEt
5c X = O, R = $(N(Me)CH_2)_2$
5d X = S, R = OEt

Entry	1	PhSH (equiv)	5[a]	Yield (%)	*E*/*Z*
1	**1d**	1.1	**5a**	72	3:7
2	**1d**	0.4	**5a**	72	3:7
3	**1e**	1.1	**5b**	Traces	—
4	**1e**	0.4	**5b**	Traces	—
5	**1f**	1.1	**5c**	Traces	—
6	**1f**	0.4	**5c**	Traces	—
7	**1g**	1.1	**5d**	78	1:1
8	**1g**	0.4	**5d**	65	1:1

[a] Reactions were conducted according to the same procedure: PhSH, AIBN (0.2 equiv), slow addition (0.15 mmol h^{-1}), Tol. reflux.

3.2. Extension to thiosulfonylations

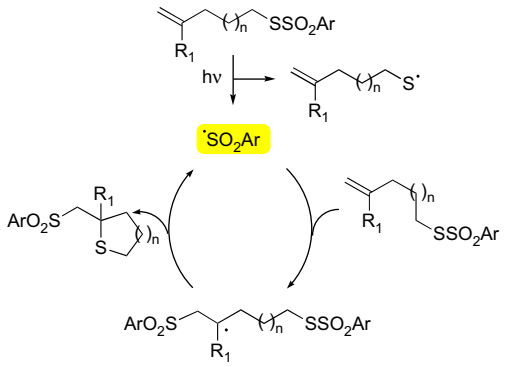
We had previously observed a dramatic change of the radical reactivity upon switching from the phosphinate to sulfinate moiety. The phosphorus tether in arylphosphinates would favor *ipso*-substitution and biaryl formation,[18] while similar sulfinates (and sulfinamides) would favor homolytic substitutions.[20] We thus decided to evaluate the behavior of thiosulfonates in the same cycloisomerization.

Such a study was also stimulated by the scarce data available in the literature for such a transformation. In a short communication, Da Silva Corrêa reported the first example of cycloisomerization of alkenyl thiosulfonate **6a** to tetrahydrothiophene **7a**.[27] Because the reaction conditions involved peroxides, we can suppose the mechanism of this rearrangement involves generation of the methylphenylsulfonyl radical, followed by addition to the double bond, intramolecular homolytic substitution of the formed β-(sulfonyl)alkyl radical at the sulfur atom, and simultaneous formation of a new methylphenylsulfonyl radical, thus a mechanism reminiscent of our thiophosphination.[28]

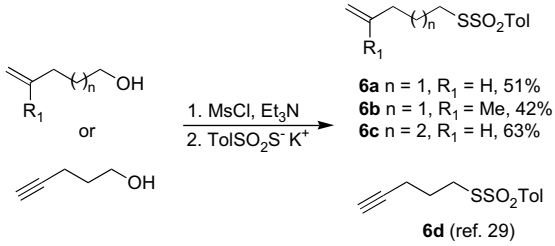
Later, it was noticed that the reaction did not require initiation by benzoyl peroxide and that leaving the samples exposed to light for one month at rt was enough to convert all the starting material to the cyclic product.[29] These results prompted us to hypothesize that the initiation step involved light-induced homolytic scission of the S–SO_2 bond, and not sacrificial addition of an initiator-derived species to a fraction of the S.M. (Scheme 9). We thus decided to reinvestigate the transformation of **6b** and try to optimize the conditions for the synthesis of the cyclic product.

The thiosulfonates **6a–d** were prepared by nucleophilic substitution of the corresponding mesylates with the potassium salt of *p*-toluenethiosulfonic acid (Scheme 10).

We first examined in more details the conditions required for the radical cycloisomerization of alkene **6a**. We carried out the cyclizations either in the presence of PhSH/AIBN in refluxing toluene, or at rt in benzene under sunlamp irradiation. Tetrahydrothiophene **7a** was isolated in similarly high yields in both cases, which validate our assumption that the S–SO_2 bond is weak enough to be easily cleaved by irradiation, and that this constitutes the initiation step for the radical mechanism described above (Scheme 9).



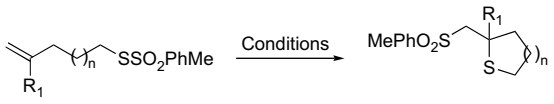
Scheme 9. Thiosulfonation of olefins.



Scheme 10. Access to the thiosulfonates.

We next looked for the scope and limitation of this reaction (Table 4). Quaternary centers could be installed (entry 4), as well as six-membered rings (entry 5). Interestingly, the cycloisomerization could also be carried out in *tert*-butanol albeit **7a** was produced in lower yield (entry 3). But the most surprising feature came from the reaction of alkyne **6d**. No conversion to the desired cycloadduct was observed, **6d** undergoing slow degradation.[30] This result is quite surprising, since sulfonyl radicals are known to add onto alkynes.[31] Maybe the rate of addition of the former cannot sustain a chain process, since it seems unlikely that the homolytic substitution step should be an unfavorable process, as was evident with thiophosphine oxides (see above). In any case, we have evidenced a new complementarity between sulfur and phosphorus. Unfortunately, it was not possible to extend this particular cycloisomerization to the formation of small or medium-sized rings.

Table 4



Entry	6	Conditions	7[a]	Yield (%)
1	**6a**	A	**7a**	86
2	**6a**	B	**7a**	82
3	**6a**	C	**7a**	70
4	**6b**	B	**7b**	86
5	**6c**	B	**7c**	86

[a] Method A: PhSH (1.1 equiv), AIBN (0.2 equiv), slow addition (0.15 $mmol^{-1}$), Tol. reflux. Method B: Sunlamp irradiation (300 W) for 1 h in PhH (0.03 mol/l). Method C: same as Method B with *t*-BuOH (0.03 mol/l).

4. Conclusion

In summary we have devised two efficient approaches for the formation of *P*(V)-centered radicals from aryl or alkyne thiophosphonates with and without tin hydride. The *P*-centered radicals that were generated could be engaged in several bond forming process, and efficient cycloisomerizations were carried out, which led to the bis-functionalization of alkenes and alkynes. The scope of the thiosulfonation of olefins was extended, while an unprecedented thiophosphination of alkynes was introduced. During the course of this work, we evidenced a complementary reactivity of sulfur- and phosphorus-containing functions. We believe these reactions to be of interest for the synthesis of sulfur heterocycles.

5. Experimental

5.1. General remarks

Reagents and chemicals were purchased from commercial sources and used as received. Reactions were carried out under argon, with magnetic stirring and degassed solvents. CH_2Cl_2, benzene, and toluene were dried and distilled from CaH_2. Thin-layer chromatography (TLC) was performed on Merck 60 F_{254} silicagel. Merck Geduran SI 60 Å silicagel (35–70 mm) was used for column chromatography. The melting points reported were measured with a Reichert hot-stage apparatus and are uncorrected. IR spectra were recorded from a Bruker Tensor 27 ATR diamond PIKE spectrometer. ^1H NMR [^{13}C NMR] spectra were recorded at rt with a 400 MHz [100 MHz] Bruker AVANCE 400 spectrometer or a 200 MHz [50 MHz] Bruker AVANCE 200. Chemical shifts are given in parts per million, referenced to TMS (δ=0 ppm) using the solvent signals (δ=7.28 or 77.16, respectively, for $CDCl_3$). Coupling constants (*J*) are given in hertz (Hz). ^{31}P NMR spectra were obtained at 298 K in 5 mm o.d. tube at 162 MHz, on a Bruker AVANCE 400 spectrometer equipped with a QNP or BBFO probe at a concentration of 100 mg/0.5 mL. External 85% H_3PO_4 in coaxial tube was used as reference. Exact masses were recorded at the Institut de chimie moléculaire (FR 2769) of our University (electrospray source). Elemental analyses were performed by ICSN (CNRS, Gif).

5.2. GP1: preparation of the thiophosphonates and related compounds

To the starting thiol (5 mmol) in THF (30 mL) at 0 °C was added NaH (60% in mineral oil, 6 mmol, 240 mg). The $R_2P(=O)Cl$ derivative (6 mmol) was added after 5 min and the reaction was left at rt until completion, as monitored by TLC. The reaction mixture was diluted with Et_2O (15 mL), washed with satd aq NH_4Cl, water, and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude products were purified by flash column chromatography (silicagel).

5.3. GP2: preparation of the thiophosphonates from sulfonates

To the starting sulfonate (15 mmol) in degassed DMF (150 mL) was added $NH_4SP(=S)(OEt)_2$ (18 mmol, 3.66 g) and the reaction was heated overnight at 50 °C. After completion (TLC monitoring), the reaction mixture was diluted with CH_2Cl_2 (80 mL), washed with water (×4), and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude products were purified by flash column chromatography (silicagel).

5.4. GP3: tributyltin hydride-mediated formation of C–P bonds

A degassed solution of AIBN (0.012 mmol, 15 mol %, 15 mg) and Bu_3SnH (0.6 mmol, 0.16 mL) in toluene (5 mL) was added via syringe pump (0.2 mmol h^{-1}) to a refluxed, degassed solution of the thiophosphonyl substrate (0.5 mmol), the alkene (5 or 10 equiv), and AIBN (0.04 mmol, 5 mol %, 5 mg) in toluene (12 mL). After completion of the addition, the reaction mixture was refluxed for an additional hour, and concentrated. Flash column chromatography (silicagel) delivered the expected products.

5.5. GP4: catalytic tin conditions

A degassed solution of the thiophosphonyl derivative (0.5 mmol), Bu_3SnCl (0.06 mmol, 10 mol %, 0.16 mL), $NaBH_4$ (1 mmol, 38 mg), the alkene (1 mmol), and AIBN (0.05 mmol, 10 mol %, 9 mg) in *tert*-butanol (25 mL) was refluxed for 5 h (AIBN (0.05 mmol, 10 mol %, 9 mg) was added again after 2.5 h.). After completion, the reaction mixture was treated with satd aq NH_4Cl. The aqueous phase was extracted with Et_2O (3×15 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude products were purified by flash column chromatography (silicagel).

5.6. GP5: thiophenol-mediated formation of C–P bonds, and cycloisomerizations

A degassed solution of AIBN (0.1 mmol, 20 mol %, 16 mg) and thiophenol (0.55 mmol (or 0.2 mmol for cycloisomerizations), 56 μl (respectively, 20 μl) in toluene (8 mL)) was added via syringe pump (0.15 mmol h^{-1}) to a refluxed and degassed solution of the alkynyl thiophosphonyl substrates (0.5 mmol) and alkene (0 for cycloisomerizations, 5 or 10 equiv) in toluene (8 mL). After completion of the addition, the reaction mixture was refluxed for an additional hour, and concentrated. Flash column chromatography (silicagel) delivered the expected products.

5.7. GP6: preparation of the thiosulfonates

To the starting sulfonate (15 mmol) in degassed DMF (150 mL) was added $MePhSO_2SK$ (18 mmol, 4.07 g) and the reaction mixture was heated overnight at 50 °C. After completion (TLC monitoring), the reaction mixture was diluted with CH_2Cl_2 (80 mL), washed with water (×4), and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude products were purified by flash column chromatography (silicagel).

5.8. GP7: light-promoted cycloisomerization of thiosulfonates

A degassed solution of the thiosulfonate substrate (0.5 mmol) in benzene (15 mL) was irradiated to reflux with a sunlamp (300 W). After completion, the solvent was evaporated. Flash column chromatography (silicagel) delivered the expected products.

5.9. 2-(2′-Bromophenyl)ethanol

To a solution of 2-bromophenyl acetic acid (4.95 g, 23 mmol) in THF (25 mL) was added dropwise at 5 °C a $BH_3{\cdot}SMe_2$ complex solution 2 M in THF (25 mL, 25 mmol). The reaction mixture was left at 5 °C for 30 min, allowed to warm to rt overnight, and slowly poured into ice-cold methanol (100 mL) with gentle swirling and left to stand for at least 6 h. The clear solution was then concentrated and the residue was dissolved in Et_2O (100 mL). The organic layer was washed with satd $NaHCO_3$ (3×50 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude alcohol was isolated in 95% yield (4.4 g) as a colorless oil. Spectral data corresponded to those reported in the literature (CAS number: 1074-16-4).[32]

5.10. 2-Bromophenethyl methanesulfonate

Methanesulfonyl chloride (2.7 mL, 35 mmol) was added dropwise over 5 min to a cooled (0 °C) solution of 2-(2′-bromophenyl)-ethanol (4.5 g, 23 mmol) and triethylamine (6.5 mL, 46 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was further stirred at 0 °C for 5 min, then at rt for 2 h. It was quenched with H_2O, and the organic layer was washed with water (2×50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude sulfonate was used without further purification. Spectral data corresponded to those reported in the literature (CAS number: 2183-83-7).[32]

5.11. *S*-2-Bromophenethyl ethanethioate

To a solution of 2-(2′-bromophenyl)ethanol (4.73 g, 23.4 mmol) in 150 mL of THF were added successively PPh_3 (9.26 g, 35.1 mmol) and DEAD (40% in toluene, 16.2 mL, 35.1 mmol) at rt. After 5 min, AcSH (3.36 mL, 46.8 mmol) was added dropwise to the solution, which turned yellow (from light green). The mixture was stirred overnight at rt. After partial evaporation of the solvent (to approx. 50 mL), *n*-pentane (100 mL) was added to precipitate triphenylphosphine oxide. The white solid was filtered off and the filtrate was concentrated in vacuo. The crude material was purified by flash column chromatography (CH_2Cl_2/petroleum ether 1:3) to give the title compound in 72% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36 (s, 3H, MeCO), 3.02 (m, 2H, CH_2CH_2S), 3.16 (m, 2H, CH_2S), 7.11 (m, 1H arom.), 7.28 (m, 2H arom.), 7.55 (dd, J=8.0 Hz, 1.0 Hz, 1H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.8 (*Me*CO), 30.7 (CH_2CH_2S), 36.0 (CH_2S), 124.4 (C arom.), 127.5 (CH arom.), 128.3 (CH arom.), 130.8 (CH arom.), 132.9 (CH arom.), 139.1 (C arom.), 195.6 (CO).

The isolated sulfonate (6.14 g, 22 mmol) was added to cesium thioacetate (23.1 mmol)—which was prepared by addition of Cs_2CO_3 (7.9 g, 24.2 mmol) to a solution of freshly distilled thioacetic acid (1.65 mL, 23.1 mmol) in MeOH (40 mL) followed by concentration in vacuo—in dry DMF (100 mL). The mixture was heated with stirring at 50 °C for 20 h, then cooled and diluted with CH_2Cl_2 (150 mL). DMF was removed by repeated washings with water (4×50 mL). Filtration of the crude product through a short silicagel plug gave the title compound in 70% yield (4 g, 15.4 mmol) as an oil.

5.12. 2-(2′-Bromophenyl)ethanethiol

To a solution of thioacetate (1.9 g, 7.3 mmol) in Et_2O (50 mL) at −78 °C was added a solution of Dibal-H (1 M in hexanes, 18.3 mL, 18.3 mmol) over 15 min. The solution was allowed to warm to rt and further reacted for two more hours. The reaction mixture was quenched with 3 M HCl and the organic layer was washed with satd aq $NaHCO_3$, water and brine, then dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (petroleum ether) to yield the thiol (1.44 g, 6.64 mmol, 91%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.43 (t, J=15.6 Hz, 1H, SH), 2.40 (m, 2H, CH_2S), 3.10 (m, 2H, CH_2CH_2S), 7.12 (m, 1H arom.), 7.27 (m, 2H arom.), 7.56 (d, J=15.4 Hz, 1H arom.).

5.13. Compound 1a

Following GP1 from 2-(2′-bromophenyl)ethanethiol (1.06 g, 5 mmol) and diphenylphosphinic chloride (1.42 g, 6 mmol), substrate **1a** was isolated (petroleum ether/ethyl acetate 2:1, 1.71 g, 82%) as a colorless dense oil. IR (neat): 3056, 2927, 1589, 1568, 1113 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.05–3.10 (m, 4H, CH_2CH_2), 7.05–7.10 (m, 1H arom.), 7.16–7.25 (m, 2H arom.), 7.47–7.60 (m, 7H

arom.), 7.88–7.92 (m, 4H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.6 (d, J=2.2 Hz, ArCH_2), 37.3 (d, J=4.4 Hz, SCH_2), 124.3 (C arom.), 127.5 (CH arom.), 128.4 (CH arom.), 128.7 (d, J=10.3 Hz, CH arom.), 131.1 (CH arom.), 131.5 (d, J=10.3 Hz, CH arom.), 132.4 (d, J=2.6 Hz, CH arom.), 132.9 (CH arom.), 133.2 (d, J=106.2 Hz, =CP), 138.7 (C arom.). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 44.6. Elemental analysis (%) for $C_{20}H_{18}BrOPS$ (417.30): calcd. C 57.56, H 4.35; found C 57.12, H 4.43. HRMS calcd for $C_{20}H_{18}^{81}BrONaPS$ ([M+Na]$^+$): 440.9877, found 440.9840.

5.14. Compound 1b

Following GP1 from 2-(2′-bromophenyl)ethanethiol (1.06 g, 5 mmol) and diethyl chlorophosphate (1.035 g, 6 mmol), substrate **1b** was isolated (petroleum ether/ethyl acetate 2:1, 1.16 g, 66%) as a colorless oil. IR (neat): 2981, 2927, 1010 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, J=7.1 Hz, 6H, OCH_2Me), 2.99–3.11 (m, 4H, CH_2CH_2), 4.06–4.20 (m, 4H, OCH_2Me), 7.04–7.10 (m, 1H arom.), 7.20–7.29 (m, 2H arom.), 7.49–7.51 (m, 1H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.1 (d, J=7.7 Hz, OCH_2Me), 30.1 (ArCH_2), 37.4 (d, J=5.1 Hz, SCH_2), 63.5 (d, J=5.1 Hz, OCH_2Me), 124.3 (C arom.), 127.6 (CH arom.), 128.5 (CH arom.), 131.0 (CH arom.), 132.9 (CH arom.), 138.6 (C arom.). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 28.9. Elemental analysis (%) for $C_{12}H_{18}BrO_3PS$ (353.21): calcd. C 40.81, H 5.14; found C 40.65, H 5.26. HRMS calcd for $C_{12}H_{18}^{81}BrO_3NaPS$ ([M+Na]$^+$): 376.9775, found 376.9764.

5.15. Compound 1c

Following GP1 from 2-(2′-bromophenyl)ethanethiol (1.06 g, 5 mmol) and 1,3-dimethyl-2-oxo-1,3,2-diazaphospholidine (1.01 g, 6 mmol), substrate **1c** was isolated (petroleum ether/ethyl acetate 1:1, 978 mg, 56%) as a whitish dense oil. IR (neat): 2986, 2928, 1159 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56 (d, J=8.3, 1H), 2.68 (s, 3H, NMe), 2.71 (s, 3H, NMe), 2.86–2.93 (m, 2H, CH_2), 3.05–3.08 (m, 2H, CH_2), 3.12–3.18 (m, 2H, CH_2), 3.30–3.36 (m, 2H, NCH_2), 7.10–7.14 (m, 1H arom.), 7.25–7.29 (m, 2H arom.), 7.54–7.56 (m, 1H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 30.2 (d, J=4.3 Hz, CH_2Ar), 31.3 (d, J=6.0 Hz, NMe), 37.6 (d, J=5.1 Hz, CH_2S), 47.6 (d, J=9.4 Hz, NCH_2), 124.2 (C arom.), 127.6 (CH arom.), 128.4 (CH arom.), 131.1 (CH arom.), 132.9 (CH arom.), 139.1 (C arom.). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 42.1. Elemental analysis (%) for $C_{12}H_{18}BrN_2OPS$ (349.23): calcd C 41.27, H 5.20, N 8.02; found C 40.94, H 5.22, N 7.94.

5.16. Synthesis of the acyclic alkenyl or alkynyl thiols

Methanesulfonylchloride (3.48 mL, 45 mmol) was added over 5 min at 0 °C to a stirred solution of alcohol (30 mmol) and triethylamine (8.43 mL, 60 mmol) in CH_2Cl_2 (200 mL). After 5 min at 0 °C and 2 h at rt, the reaction mixture was washed with water (2×50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo.

The crude sulfonate (30 mmol) was used without purification. It was added to cesium thioacetate (31.5 mmol)—which was prepared by addition of Cs_2CO_3 (10.75 g, 33 mmol) to a solution of freshly distilled thioacetic acid (2.25 mL, 31.5 mmol) in MeOH (60 mL) followed by concentration in vacuo—in dry DMF (190 mL). The reaction mixture was heated at 50 °C for 20 h, then diluted with CH_2Cl_2 (200 mL). DMF was removed by repeated washings with water (4×50 mL). The combined organics were concentrated in vacuo. The crude product was filtered through a short plug of silicagel, delivering the title compound as an oil.

To a suspension of K_2CO_3 (11 mmol, 1.1 equiv) in MeOH (60 mL) stirred 20 min at rt, was added the crude thioacetate (10 mmol). The evolution of reaction was monitored by TLC. After 20 min of stirring, the reaction mixture was quenched with 0.1 M HCl (180 mL) and extracted with CH_2Cl_2 (4×30 mL). The organic layer was washed with aq NaCl, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was used without purification.

5.17. Pent-4-ynyl methanesulfonate

Starting from pent-4-yn-1-ol (2.52 g, 30 mmol), the corresponding sulfonate was isolated without purification (4.87 g, >98%) as a brown dense oil. Spectral data corresponded to those reported in the literature (CAS number: 68275-03-6).[33]

5.18. Pent-4-enyl methanesulfonate

Starting from pent-4-en-1-ol (860 mg, 10 mmol), the corresponding sulfonate was isolated without purification (1.64 g, >98%) as a brown dense oil. Spectral data corresponded to those reported in the literature (CAS number: 64818-35-5).[34]

5.19. *S*-Pent-4-ynyl ethanethioate

Starting from pent-4-ynyl methanesulfonate (4.87 g, 30 mmol), the corresponding thioacetate was isolated without purification (3.41 g, 80%) as a clear oil. Spectral data corresponded to those reported in the literature (CAS number: 64818-35-5).[25a]

5.20. *S*-Pent-4-enyl ethanethioate

Starting from pent-4-enyl methanesulfonate (3.28 g, 20 mmol), the corresponding thioacetate was isolated without purification (2.51 g, 87%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64 (quint., J=6.9 Hz, 2H, $CH_2CH_2CH_2$), 2.12 (q, J=6.9 Hz, 2H,C=C–CH_2), 2.32 (s, 3H, COMe), 2.87 (t, J=6.8 Hz, 2H, CH_2S), 5.00 (m, 2H, HC=CH_2), 5.77 (m, 1H, HC=CH_2).

5.21. Pent-4-yne-1-thiol

Starting from *S*-pent-4-ynyl ethanethioate (3.41 g, 24 mmol), the corresponding thiol was isolated without purification (1.4 g, 56%) as a clear oil. Spectral data corresponded to those reported in the literature (CAS number: 77213-88-8).[25a]

5.22. Pent-4-ene-1-thiol

Starting from *S*-pent-4-enyl ethanethioate (1.44 g, 10 mmol), a 65:35 mixture of the corresponding thiol and disulfide was isolated without purification (612 mg, 60%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J=8.0 Hz, 1H, SH), 1.72 (m, 2H, $CH_2CH_2CH_2$), 2.24–2.07 (m, 2H, =CHCH_2), 2.55 (td, J=7.8 Hz, 7.8 Hz, 2H, CH_2S), 5.0 (m, 2H), 5.8 (m, 1H) (CAS number: 17651-37-5).

5.23. Compound 1d

Following GP1 from pent-4-yne-1-thiol (500 mg, 5 mmol), substrate **1d** was isolated (petroleum ether/ethyl acetate 1:1, 978 mg, 56%) as a whitish dense oil. IR (neat): 3295, 3056, 2926, 2117, 1588, 1194 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85 (quint., J=7.1 Hz, 2H, SCH_2CH_2), 1.90 (t, J=2.7 Hz, 1H, ≡CH), 2.25 (td, J=7.1, 2.7 Hz, 2H, ≡CCH_2), 2.91 (dt, J=11.4, 7.1 Hz, 2H, SCH_2), 7.43–7.56 (m, 6H, arom.), 7.84–7.91 (m, 4H, arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.3 (SCH_2CH_2), 28.2 (≡CCH_2), 29.2 (d, J=4.3 Hz, SCH_2), 69.3 (≡CH), 82.7 (≡CCH_2), 128.7 (d, J=12.8 Hz, CH arom.), 131.5 (d, J=10.3 Hz, CH arom.), 132.4 (d, J=3.4 Hz, CH arom.), 133.2 (d, J=106.3 Hz, C arom.). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 44.6 (CAS number: 934538-84-8).

5.24. Compound 1e

Following GP1 from pent-4-yne-1-thiol (500 mg, 5 mmol), substrate **1e** was isolated (petroleum ether/ethyl acetate 1:1, 602 mg, 51%) as a yellow oil. IR (neat): 3232, 2982, 2117, 1162 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, J=7.1 Hz, 6H, OCH_2Me), 1.90 (quint., J=7.1 Hz, 2H, SCH_2CH_2), 1.96 (t, J=2.7 Hz, 1H, ≡CH), 2.31 (td, J=7.1, 2.7 Hz, 2H, ≡CCH_2), 2.93 (dt, J=11.4, 7.1 Hz, 2H, SCH_2), 4.05–4.22 (m, 4H, OCH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.1 (d, J=6.9 Hz, OCH_2Me), 17.3 (SCH_2CH_2), 29.4 (d, J=4.8 Hz, SCH_2 or ≡CCH_2), 29.6 (d, J=4.3 Hz, SCH_2 or ≡CCH_2), 63.5 (d, J=6.0 Hz, OCH_2), 69.3 (≡CH), 82.7 (≡CCH_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 29.0 (CAS number: 934538-85-9).

5.25. Compound 1f

Following GP1 from pent-4-yne-1-thiol (500 mg, 5 mmol), substrate **1f** was isolated (CH_2Cl_2/MeOH 9:1, 488 mg, 42%) as a yellow oil. IR (neat): 3213, 2928, 1475, 1160 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.83 (quint., J=7.1 Hz, 2H, SCH_2CH_2), 1.96 (t, J=2.7 Hz, 1H, ≡CH), 2.31 (td, J=7.1, 2.7 Hz, 2H, ≡CCH_2), 2.68 (s, 3H, NMe), 2.71 (s, 3H, NMe), 2.73 (td, J=11.4, 7.1 Hz, 2H, SCH_2), 3.05–3.14 (m, 2H, NCH_2), 3.27–3.37 (m, 2H, NCH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.4 (SCH_2CH_2), 29.5 (d, J=5.1 Hz, SCH_2 or ≡CCH_2), 29.6 (d, J=4.3 Hz, SCH_2 or ≡CCH_2), 31.3 (d, J=6.0 Hz, NCH_2), 47.5 (d, J=10.3 Hz, NMe), 69.1 (≡CH), 83.1 (≡CCH_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 42.0 (CAS number: 934538-86-0).

5.26. Compound 1g

Following GP2 from pent-4-ynyl methanesulfonate (810 mg, 5 mmol), substrate **1g** was isolated (petroleum ether/ethyl acetate 9:1, 676 mg, 53%) as a yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.39 (t, J=7.4 Hz, 6H, 2 CH_3), 1.83 (quint., J=7.4 Hz, 2H, SCH_2CH_2), 2.01 (t, J=2.7 Hz, 1H, ≡CH), 2.34 (dt, J=7.0, 1.3 Hz, 2H, ≡CCH_2), 3.00 (td, J=16.4, 7.4 Hz, 2H, SCH_2), 4.23 (m, 4H, $2OCH_2$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.9 (d, J=8.6 Hz, CH_3), 17.4 (SCH_2CH_2), 29.0 (d, J=4.3 Hz, ≡CCH_2), 32.2 (d, J=4.3 Hz, SCH_2), 63.9 (d, J=8.6 Hz, OCH_2), 69.4 (≡CH), 82.7 (≡CCH_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 96.8.

5.27. Compound 1h

Following GP1 from pent-4-ene-1-thiol (612 mg, 6 mmol), substrate **1h** was isolated (petroleum ether/ethyl acetate 1:1, 800 mg, 44%) as a whitish dense oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.70 (quint., J=7.4 Hz, 2H, SCH_2CH_2), 2.08–2.12 (m, 2H, CH_2CH=), 2.81 (dt, J=10.6, 7.4 Hz, 2H, SCH_2), 4.91 (m, 2H), 5.65 (m, 1H), 7.40–7.56 (m, 6H arom.), 7.81–7.91 (m, 4H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.6 (CH_2CH_2), 29.7 (CH_2=$CHCH_2$), 32.5 (d, J=4.3 Hz, SCH_2), 115.6 (CH_2=CH), 128.6 (d, J=12.8 Hz, CH arom.), 131.4 (d, J=10.3 Hz, CH arom.), 132.3 (d, J=3.4 Hz, CH arom.), 133.1 (d, J=106.3 Hz, C arom.), 137.1 (CH_2=CH). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 44.5.

5.28. Compound 2a

Following GP3 from **1a** (209 mg, 0.5 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), or following GP4 from **1a** (209 mg, 0.5 mmol) and 1-octene (112 mg, 1 mmol, 2 equiv), or following GP5 from **1d** (292 mg and 290 mg, 0.973 mmol and 0.966 mmol) and 1-octene (217 mg and 1.09 g, 1.94 mmol and 9.73 mmol, 2 equiv and 10 equiv), adduct **2a** was isolated as a white solid (petroleum ether/ethyl acetate 50:50, 132 mg (respectively, 91 mg, 168 mg and 252 mg), 84% (respectively, 58%, 57%, and 87%)). Mp 57–58.5 °C. IR (neat): 3055, 2924, 2853, 1181, 1119 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, J=7.1 Hz, 3H, Me), 1.18–1.31 (m, 8H, CH_2), 1.35–1.44 (m, 2H, CH_2), 1.57–1.66 (m, 2H, CH_2), 2.22–2.30 (m, 2H, CH_2), 7.44–7.53 (m, 6H arom.), 7.71–7.78 (m, 4H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (Me), 21.4 (d, J=3.4 Hz, $PCH_2CH_2CH_2$), 22.6 (CH_2), 29.0 (CH_2), 29.7 (d, J=71.1 Hz, PCH_2), 31.0 (d, J=14.6 Hz, PCH_2CH_2), 31.8 (CH_2), 128.6 (d, J=12.0 Hz, CH arom.), 130.8 (d, J=9.4 Hz, CH arom.), 131.6 (d, J=3.4 Hz, CH arom.), 133.2 (d, J=96.8 Hz, C arom.). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 34.1. HRMS calcd for $C_{20}H_{28}OP$ (MH^+): 315.1878, found 315.1878.

5.29. Compound 2b

Following GP3 from **1b** (176 mg, 0.5 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), or following GP4 from **1b** (176 mg, 0.5 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), or following GP5 from **1e** (150 mg and 213 mg, 0.63 mmol and 0.96 mmol) and 1-octene (141 mg or 1.01 g, 1.26 mmol and 9 mmol, 2 equiv or 10 equiv), adduct **2b** was isolated as a colorless oil (CH_2Cl_2/ethyl acetate 50:50, 94 mg (respectively, 87 mg, 45 mg and 130 mg), 75% (respectively, 70%, 29%, and 58%)). Its spectral data correspond to those of commercial samples (CAS number: 1068-07-1).

5.30. Compound 2c

Following GP3 from **1c** (113 mg, 0.323 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), or following GP4 from **1c** (175 mg, 0.5 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), or following GP5 from **1f** (116 mg, 0.5 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), adduct **2c** was isolated as a colorless oil contaminated by approx. 50% of by-products (CH_2Cl_2/methanol 90:10, 50 mg (respectively, 59 mg and 113 mg), 62% (respectively, 48% and ~40% yield estimated by ^1H NMR ratio)). IR (neat): 2923, 2853, 1156 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J=7.1 Hz, 3H, Me), 1.18–1.37 (m, 12H, CH_2), 1.76–1.84 (m, 2H, CH_2P), 2.66 (d, J=9.4 Hz, 6H, NMe), 3.04–3.08 (m, 2H, NCH_2), 3.16–3.23 (m, 2H, NCH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (CH_3), 22.6 (CH_2), 23.0 (d, J=4.3 Hz, CH_2), 26.9 (d, J=115.7 Hz, PCH_2), 29.0 (CH_2), 29.1 (CH_2), 30.7 (d, J=17.1 Hz, CH_2), 31.7 (CH_2), 31.9 (d, J=5.1 Hz, NMe), 48.3 (NCH_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 43.3. HRMS calcd for $C_{12}H_{28}N_2OP$ ($[M+H]^+$): 247.1939, found 247.1934.

5.31. Compound 2d

Following GP5 from **1g** (126 mg, 0.5 mmol) and 1-octene (561 mg, 5 mmol, 10 equiv), adduct **2d** was isolated as an oil (petroleum ether/ethyl acetate 80:20, 123 mg, 93%). Spectral data corresponded to those reported in the literature (CAS number: 100543-37-1).[23e]

5.32. Compound 3a

Following GP3 from **1a** (209 mg, 0.5 mmol) and acrylonitrile (53 mg, 5 mmol, 10 equiv), or following GP4 from **1a** (209 mg, 0.5 mmol) and acrylonitrile (53 mg, 1 mmol, 2 equiv), or following GP5 from **1d** (150 mg, 0.5 mmol) and acrylonitrile (53 mg, 1 mmol, 2 equiv), adduct **3a** was isolated as an oil contaminated by approx. 20% of by-products (petroleum ether/ethyl acetate 50:50, 45 mg (respectively, 64 mg and 85 mg), 39% (respectively, 50% and 66% (contaminated by approx. 30% of an undefined product))). Spectral data corresponded to those reported in the literature.[35]

5.33. Compound 3b

Following GP3 from **1b** (176 mg, 0.5 mmol) and acrylonitrile (265 mg, 5 mmol, 10 equiv), adduct **3b** was isolated (ethyl acetate, 71 mg, 74%) as a colorless oil. Its spectral data corresponded to those of commercial samples (CAS number: 10123-62-3).[36]

5.34. Compound 3c

Following GP3 from **1c** (113 mg, 0.323 mmol) and acrylonitrile (64 mg, 1 mmol, 2 equiv), or following GP5 from **1f** (116 mg, 0.5 mmol) and acrylonitrile (106 mg, 2 mmol, 4 equiv), adduct **3c** was isolated as a white solid (CH_2Cl_2/methanol 90:10, 50 mg (respectively, 42 mg), 82% (respectively, 45%)). Mp 112–115 °C. IR (neat): 2912, 2866, 2361, 1168 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.16 (dt, J=15.4, 7.8 Hz, 2H, CH_2), 2.47 (dt, J=15.6, 7.8 Hz, 2H, CH_2), 2.67 (d, J=9.6 Hz, 6H, NMe), 3.12–3.26 (m, 4H, NCH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.3 (d, J=4.3 Hz, *C*H_2CN), 22.4 (d, J=120.0 Hz, CH_2P), 31.6 (d, J=5.1 Hz, NMe), 47.9 (d, J=9.4 Hz, NCH_2), 119.0 (CN). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 37.4. HRMS calcd for $C_7H_{14}N_3OPNa$ ($[M+Na]^+$): 210.0772, found 210.0782.

5.35. Compound 3d

Following GP5 from **1g** (126 mg, 0.5 mmol) and acrylonitrile (133 mg, 2.5 mmol, 5 equiv), adduct **3d** was isolated as a white solid (petroleum ether/ethyl acetate 90:10, 50 mg, 48%). ^1H NMR ($CDCl_3$, 400 MHz): δ 1.30 (t, J=7.5 Hz, 6H, 2*C*$H_3$$CH_2$), 2.25 (dt, J=15.4, 7.5 Hz, 2H, *C*H_2CN), 2.65 (dt, J=15.4, 7.5 Hz, *C*H_2P), 4.07–4.16 (m, 4H, 2O*C*H_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.6 (2 *C*$H_3$$CH_2$O), 15.8 (d, J=6.5 Hz, *C*H_2CN), 30.5 (d, J=116.5 Hz, CH_2P), 62.6 (d, J=12 Hz, 2O*C*H_2), 118.53 (d, J=18.8 Hz, CN). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 93.8. Its spectral data corresponded to those of commercial samples (CAS number: 10123-62-3).[37]

5.36. Compound 4a

Following GP3 or GP4 from **1a** (209 mg, 0.5 mmol) and *tert*-butylvinylether (500 mg, 5 mmol, 10 equiv) or following GP5 from **1d** (150 mg, 0.5 mmol) and *tert*-butylvinylether (250 mg, 2.5 mmol, 5 equiv), adduct **4a** was isolated (petroleum ether/ethyl acetate 50:50, 107 mg (respectively, 71 mg or 95 mg), 71% (contaminated by approx. 20% of an undefined by-product) (respectively, 47%) (contaminated by approx. 10% of an undefined by-product) or 63% (contaminated by approx. 42% of $Ph_2P(O)CH_2CHO$)). IR (neat): 3055, 2972, 1187, 1118 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.07 (s, 9H, C*Me*$_3$), 2.53–2.66 (m, 2H, CH_2P), 3.66–3.78 (m, 2H, CH_2O), 7.45–7.55 (m, 6H arom.), 7.70–7.78 (m, 4H arom.). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 27.7 (C*Me*$_3$), 32.0 (d, J=70.6 Hz, PCH_2), 55.6 (CH_2O), 73.9 (*C*Me$_3$), 128.9 (d, J=11.9 Hz, CH arom.), 131.1 (d, J=9.6 Hz, CH arom.), 132.0 (d, J=2.9 Hz, CH arom.), 133.7 (d, J=99.1 Hz, C arom.). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 33.2.

5.37. Compound 4b

Following GP4 from **1b** (176 mg, 0.5 mmol) and *tert*-butylvinylether (500 mg; 5 mmol; 10 equiv), adduct **4b** was isolated (CH_2Cl_2/MeOH 90:10, 67 mg, 56%) as an oil. Spectral data corresponded to those reported in the literature (CAS number: 19462-38-5).[38]

5.38. Compound 4c

Following GP3 from **1c** (175 mg, 0.5 mmol) and *tert*-butylvinylether (500 mg, 5 mmol, 10 equiv) or following GP5 from **1f** (150 mg, 0.5 mmol) and *tert*-butylvinylether (250 mg, 2.5 mmol, 5 equiv), adduct **4c** was isolated as an unstable oil (ethyl acetate/methanol 90:10, 47 mg (respectively, 100 mg), 40% (respectively, ~40% yield estimated by ^1H NMR ratio)). ^1H NMR (MeOD, 200 MHz): δ 1.23 (s, 9H, CMe_3), 2.13 (dt, J=15.6, 6.4 Hz, 2H, CH_2P), 2.68 (d, J=9.8 Hz, 6H, NMe), 3.16–3.26 (m, 4H, CH_2N), 3.56 (dt, J=18.6, 6.4 Hz, 2H, CH_2O). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 40.5. ES-MS (MeOH/CH_2Cl_2): 257.2 ($[M+Na]^+$, 100), 235.2 (MH^+, 22).

5.39. Compound 4d

Following GP5 from **1g** (126 mg, 0.5 mmol) and *tert*-butylvinylether (250 mg, 2.5 mmol, 5 equiv), adduct **4d** was isolated as an oil (petroleum ether/ethyl acetate 90:10, 77 mg, 61%). ^1H NMR ($CDCl_3$, 400 MHz): δ 1.19 (s, 9H, C*Me*$_3$), 1.29 (t, J=7.5 Hz, 6H, *C*$H_3$$CH_2$), 2.25 (dt, J=7.0, 1.6 Hz, 2H, *C*H_2P), 3.67 (dt, J=6.5, 1.6 Hz, 2H, O*C*$H_2$$CH_2$), 4.07–4.16 (m, 4H, 2O$CH_2$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.2 (*C*$H_3$$CH_2$), 27.5 (C*Me*$_3$), 35.5 (d, J=70.6 Hz, P*C*H_2), 56.3 (CH_2*C*H_2O), 62.3 (2O*C*H_2), 73.4 (*C*Me$_3$). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 97.4. Mass (M+Na): 277.1027. Elemental analysis (%) for $C_{10}H_{23}O_3PS$: calcd C, 47.23; H, 9.12; found C 47.51, H 9.01.

5.40. Compound 5a

Following GP5 from **1d** (190 mg, 0.63 mmol) and PhSH (0.071 mL, 0.69 mmol) and from **1d** (283 mg, 0.9 mmol) and PhSH (0.036 mL, 0.36 mmol, 40 mol %), product **5a** was isolated as a 70:30 *E*/*Z* mixture of isomers (petroleum ether/ethyl acetate 50:50, 194 mg, 72%). IR (neat): 3051, 2928, 1565, 1174 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.03 (quint., J=6.6 Hz, 2H, *C*$H_2$$CH_2$S, *Z*), 2.10 (quint., J=6.6 Hz, 2H, *C*$H_2$$CH_2$S, *E*), 2.87 (tdd, J=6.6, 3.0, 1.5 Hz, 2H, =CCH_2, *Z*), 2.98 (tdd, J=6.6, 3.0, 1.8 Hz, 2H, =CCH_2, *E*), 3.05–3.11 (m, 2H, SCH_2, *E*+*Z*), 6.00 (br d, J=21.0 Hz, 1H, =CH, *Z*), 6.06 (dt, J=21.0 Hz, 1.8 Hz, 1H, =CH, *E*), 7.41–7.53 (m, 6H, arom., *E*+*Z*), 7.69–7.80 (m, 4H, arom., *E*+*Z*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.4 (*C*$H_2$$CH_2$S, *Z*), 30.7 (*C*$H_2$$CH_2$S, *E*), 34.3 ($SCH_2$, *E*), 35.9 ($SCH_2$, *Z*), 36.1 (d, J=19.7 Hz, =C*C*H_2, *E*), 42.0 (d, J=14.6 Hz, =C*C*H_2, *Z*), 104.4 (d, J=109.7 Hz, =CHP, *Z*), 105.3 (d, J=108.0 Hz, =CHP, *E*), 128.4 (d, J=10.0 Hz, CH arom., *Z*), 128.5 (d, J=11.1 Hz, CH arom., *E*), 130.9 (d, J=9.4 Hz, CH arom., *E*), 131.1 (d, J=10.3 Hz, CH arom., *Z*), 131.5 (br s, CH arom., *E*+*Z*), 133.9 (d, J=104.5 Hz, =CP, *Z*), 134.7 (d, J=105.4 Hz, =CP, *E*), 168.8 (=CS, *Z*), 170.4 (d, J=5.1 Hz, =CS, *E*). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 22.2 (*E*), 23.5 (*Z*). Elemental analysis (%) for $C_{17}H_{17}OPS$ (300.36): calcd C 67.98, H 5.70; found C 67.94, H 5.71.

5.41. Compound 5d

Following GP5 from **1g** (126 mg, 0.5 mmol) and PhSH (0.056 mL, 0.55 mmol) and from **1g** (126 mg, 0.5 mmol) and PhSH (0.02 mL, 0.2 mmol), product **5d** was isolated as a 50:50 *E*/*Z* mixture of isomers (petroleum ether/ethyl acetate 50:50, 99 mg (respectively, 82 mg), 78% (respectively, 65%)). Less polar isomer. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.32 (t, J=7.3 Hz, 6H, Me), 2.17 (quint., J=6.8 Hz, 2H, CH_2*C*$H_2$$CH_2$), 3.00–3.04 (m, 2H, =$CCH_2$) 3.08 (td, J=6.3, 0.7 Hz, 2H, CH_2S), 4.03–4.15 (m, 4H, OCH_2), 5.79 (dt, J=17.4, 2.0 Hz, 1H, *C*H=C). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.2 (d, J=6.8 Hz, 2Me), 30.8 (CH_2*C*$H_2$$CH_2$), 34.3 ($CH_2S$), 35.7 (d, J=6 Hz, *C*H_2CH=), 62.1 (d, J=6 Hz, 2OCH_2), 107.1 (d, J=159.3 Hz, CH_2*C*H=), 168.3 (d, J=12 Hz, *SC*=CH). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 81.2. More polar isomer. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, J=7.0 Hz, 2CH_3, 6H), 2.06 (quint., J=6.5 Hz, CH_2*C*$H_2$$CH_2$, 2H), 2.77–2.82 (m, =$CCH_2$, 2H) 3.13 (t, J=6.5 Hz, *C*H_2S, 2H), 4.07–4.16 (m, 4H, 2OCH_2), 5.73 (dt, J=16.6, 1.5 Hz, =C*H*, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.2 (d, J=7.7 Hz, 2CH_3), 28.4 (CH_2*C*$H_2$$CH_2$), 36.1 (*C*$H_2$S), 41.6 (d, J=18.8 Hz, CH_2CH=), 62.2 (d, J=6 Hz, 2O*C*H_2), 106.7 (d, J=161 Hz, CH_2CH=), 168.4 (*SC*=CH). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 82.5. Mixture of isomers. Elemental analysis: C, 42.84; H, 6.79; found C, 43.17; H, 6.72.

5.42. 4-Methyl pent-4-enyl methanesulfonate

Starting from 4-methyl pent-4-en-1-ol (550 mg, 5.5 mmol), the expected sulfonate was isolated without purification as a brown dense oil (922 mg, 94%). ^1H NMR ($CDCl_3$, 400 MHz): δ 1.64 (br s, 1H, OH), 1.74 (s, 3H, =C(*C*H_3)CH_2), 1.91 (quint., J=7.0 Hz, 2H, CH_2*C*$H_2$$CH_2$), 2.14 (t, J=7.0 Hz, 2H, =C(CH_3)*C*H_2), 3.02 (s, 3H,

SO_2CH_3), 4.24 (t, J=6.6 Hz, 2H, CH_2O), 4.72 (s, 1H, =C*H*H), 4.79 (m, 1H, =C*H*H) (CAS number: 64818-36-6).

5.43. Hex-5-enyl methanesulfonate

Starting from hex-5-en-1-ol (860 mg, 10 mmol), the expected sulfonate was isolated without purification (1.68 g, >98%) as a brown dense oil. Spectral data corresponded to those reported in the literature (CAS number: 64818-36-6).[33]

5.44. Hept-6-enyl methanesulfonate

Starting from hept-6-en-1-ol (86 mg, 0.75 mmol), the corresponding sulfonate was isolated without purification (90 mg, 94%) as a brown dense oil. Spectral data corresponded to those reported in the literature (CAS number: 64818-37-7).[33]

5.45. Compound 6a

Following GP6 from pent-4-enyl methanesulfonate (1.98 g, 12 mmol) and $MePhSO_2SK$ (2.72 g, 12 mmol), substrate **6a** was isolated as an oil (petroleum ether/ethyl acetate 80:20, 1.57 g, 51%). IR (neat): 2923, 1639, 1593, 1322, 1138, 914, 811 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.73 (quint., J=7.3 Hz, 2H, $CH_2CH_2CH_2$), 2.06–2.13 (m, 2H, =CHCH_2), 2.47 (s, 3H, Me), 3.00 (t, J=7.3 Hz 2H, CH_2S), 5.01–4.96 (m, 2H, CH_2=), 5.74–5.64 (m, 1H, CH=), 7.35 (dd, J=8.3, 0.5 Hz, 2H arom.), 7.83 (d, J=8.3 Hz, 2H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.8 (Ar*Me*), 27.8 (CH_2CH_2S), 32.4 (=CHCH_2), 35.3 (CH_2S), 116.2 (CH_2=CH), 127.1 (2C arom.), 129.9 (2C arom.), 136.7 (CH_2=*CH*), 142.0 (SSO_2C), 144.8 (*C*Me) (CAS number: 138643-62-6).

5.46. Compound 6b

Following GP6 from 4-methyl pent-4-enyl methanesulfonate (922 mg, 5.18 mmol) and $MePhSO_2SK$ (2.36 g, 10.36 mmol), substrate **6b** was isolated as an oil (petroleum ether/ethyl acetate 80:20, 589 mg, 42%). IR (neat): 2921, 1648, 1593, 1322, 1138, 889, 811 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.66 (s, 3H, =C(CH_3)CH_2), 1.76 (quint., J=7.4 Hz, $CH_2CH_2CH_2$, 2H), 2.04 (t, J=7.4 Hz 2H, CH_2S), 2.47 (s, 3H, ArCH_3), 2.99 (t, J=7.4 Hz, 2H, =C(CH_3)CH_2), 4.66 (s, 1H, =C*H*H), 4.72 (m, 1H, =C*H*H), 7.35 (d, J=8.3 Hz, 2H arom.), 7.83 (d, J=8.3 Hz, 2H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7 (ArCH_3), 22.1 (=C(CH_3)CH_2), 26.6 ($CH_2CH_2CH_2$), 35.4 (CH_2S), 36.4 (=C(CH_3)CH_2), 111.3 (CH_2=), 127.1 (2C arom), 129.9 (2C arom.), 142.1 (SSO_2C), 143.8 (=*C*(CH_3)CH_2), 144.8 (CH_3C *arom.*). HRMS calcd for $C_{13}H_{18}O_2NaS_2$ ($[M+Na]^+$): 293.0645, found 293.0640.

5.47. Compound 6c

Following GP6 from hex-5-enyl methanesulfonate (1.69 g, 9.5 mmol) and $MePhSO_2SK$ (3.65 g, 16.15 mmol), substrate **6c** was isolated as an oil (petroleum ether/ethyl acetate 80:20, 1.61 g, 63%). IR (neat): 2924, 1639, 1593, 1323, 1138, 911, 811 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.41 (quint., J=7.3 Hz, $CH_2CH_2CH_2$, 2H), 1.62 (quint., J=7.3 Hz, $CH_2CH_2CH_2$, 2H), 2.03–1.98 (m, 2H, =CHCH_2), 2.47 (s, 3H, CH_3), 3.00 (t, J=7.3 Hz 2H, CH_2S), 4.99–4.94 (m, 2H, CH_2=), 5.77–5.67 (m, 1H, CH=), 7.36 (d, J=8.3 Hz, 2H arom.), 7.83 (d, J=8.3 Hz, 2H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7 (ArCH_3), 27.7 ($CH_2CH_2CH_2$), 28.1 ($CH_2CH_2CH_2$), 32.9 (=CHCH_2), 35.9 (CH_2S), 115.1 (CH_2=CH), 127.1 (2C arom.), 129.9 (2C arom.), 137.9 (CH_2=*CH*), 142.1 (SSO_2C), 144.7 (CH_3C *arom.*). HRMS calcd for $C_{13}H_{18}O_2NaS_2$ ($[M+Na]^+$): 293.0645, found 293.0640.

5.48. Compound 6d

Following the procedure described by Edwards from pent-4-ynyl methanesulfonate. Spectral data corresponded to those reported in the literature (CAS number: 178904-43-3).[29]

5.49. Compound 7a

Following GP5 from **6b** (128 mg, 0.5 mmol) and PhSH (0.056 mL; 0.55 mmol), or following GP7 from **6b** (256 mg, 1 mmol) in PhH (30 mL), or following GP7 from **6b** (256 mg, 1 mmol) in *t*-BuOH (30 mL), adduct **7b** was isolated as a white solid (petroleum ether/ethyl acetate 80:20, 110 mg (respectively, 211 mg and 180 mg), 86% (respectively, 82% and 70%)). Spectral data corresponded to those reported in the literature (CAS number: 138643-63-7).[26] Mp :59–61 °C. Elemental analysis (%) for $C_{12}H_{16}O_2S_2$ (256.38): calcd. C 56.22, H 6.29; found C 56.28, H 6.34.

5.50. Compound 7b

Following GP7 from **6c** (135 mg, 5.18 mmol), adduct **7c** was isolated as a solid (petroleum ether/ethyl acetate 80:20, 116 mg, 86%). Mp 47 °C. IR (neat): 2927, 1596, 1314, 1141, 1085, 814 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.71 (s, 3H, SC(CH_3)CH_2), 1.96–2.02 (m, 1H, CH*H*SC(CH_3)CH_2), 2.08–2.15 (m, 2H, CH_2CH_2S), 2.24–2.31 (m, 1H, CH*H*SC(CH_3)CH_2), 2.44 (s, 3H, Ar*Me*), 2.86–2.98 (m, 2H, CH_2CH_2S), 3.46 (d, J=14.2 Hz, 1H, part A of AB system, CH_2SO_2), 3.53 (d, J=14.2 Hz, 1H, part B of AB system, CH_2SO_2), 7.36 (d, J=8.3 Hz, 2H arom.), 7.78 (d, J=8.3 Hz, 2H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7 (Ar*Me*), 29.0 (SC(CH_3)CH_2), 29.8 (CH_2CH_2S), 33.2 (CH_2CH_2S), 43.2 (CH_2SC(CH_3)CH_2), 54.7 (SC(CH_3)CH_2), 67.9 (CH_2SO_2), 127.8 (2C arom.), 129.9 (2C arom.), 138.3 (*C*Me), 144.6 (CSO_2). Elemental analysis (%) for $C_{13}H_{18}O_2S_2$ (270.07): calcd. C 57.74, H 6.71; found C 57.76, H 6.88.

5.51. Compound 7d

Following GP7 from **6d** (270 mg, 1 mmol), substrate **7d** was isolated as a white solid (petroleum ether/ethyl acetate 80:20, 232 mg, 86%). Mp: 59–61 °C. IR (neat): 2920, 1596, 1299, 1137, 1084, 813 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.36–1.47 (m, 1H, CH_2CHHCH_2), 1.54–1.66 (m, 2H, CH*H*CH(CH_2SO_2PhMe)S and CH*H*CH_2S), 1.77–1.91 (m, 2H, CH*H*CH_2S and CH*H*CH_2CH_2S), 2.26–2.32 (m, 1H, CH*H*CH(CH_2SO_2PhMe)S), 2.46 (s, 3H, ArCH_3), 2.54–2.60 (m, 1H, CH_2CH*H*S), 2.65–2.72 (m, 1H, CH_2CH*H*S), 3.15–3.30 (m, 3H, *CH*(CH_2SO_2PhMe)S and CH(CH_2SO_2PhMe)S), 7.36 (d, J=8.3 Hz, 2H arom.), 7.80 (d, J=8.3 Hz, 2H arom.). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7 (*Me*Ar), 24.9 ($CH_2CH_2CH_2S$), 26.5 (CH_2CH_2S), 29.1 (CH_2CH_2S), 33.6 (CH_2CH(CH_2SO_2PhMe)S), 35.6 (*C*H(CH_2SO_2PhMe)S), 61.3 (CH_2SO_2PhMe), 128.0 (2C arom.), 130.0 (2C arom.), 136.8 (*C*Me), 144.9 (CSO_2). Elemental analysis (%) for $C_{13}H_{18}O_2S_2$ (270.41): calcd C 57.74, H 6.71; found C 57.59, H 6.79.

Acknowledgements

We thank CNRS, IUF, UPMC, and ANR (grant BLAN0309, 'Radicaux verts') for financial support. Technical support from ICSN (Gif sur Yvette, France) is gratefully acknowledged (HRMS and elemental analyses).

References and notes

1. Renaud, P.; Sibi, M. P. *Radicals in Organic Synthesis*, 1st ed.; Wiley-VCH: Weinheim, 2001.
2. Carta, P.; Puljic, N.; Robert, C.; Dhimane, A.-L.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Org. Lett.* **2007**, *9*, 1061–1063.

3. (a) Julia, M.; Le Goffic, F.; Katz, L. *Bull. Soc. Chim. Fr.* **1964**, 1122–1128; (b) Julia, M.; Le Goffic, F. *Bull. Soc. Chim. Fr.* **1964**, 1129–1133.
4. (a) Stork, G.; Hutchinson, D.; Okabe, M.; Parker, D.; Choon Sup, R.; Ribéreau, F.; Suzuki, T.; Zebovitz, T. *Pure Appl. Chem.* **1992**, *64*, 1809–1812; (b) Stork, G.; Franklin, P. J. *Aust. J. Chem.* **1992**, *45*, 275–284.
5. Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237–1286.
6. For a survey of recent advances in cascade reactions, see: Albert, M.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Top. Curr. Chem.* **2006**, *164*, 1–62.
7. Bogen, S.; Malacria, M. *J. Am. Chem. Soc.* **1996**, *118*, 3992–3993.
8. (a) Bogen, S.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **1997**, *119*, 5037–5038; (b) Bogen, S.; Fensterbank, L.; Malacria, M. *J. Org. Chem.* **1999**, *64*, 819–825.
9. (a) Journet, M.; Malacria, M. *Tetrahedron Lett.* **1992**, *33*, 1893–1896; (b) Gulea, M.; Lopez-Romero, J. M.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2000**, *2*, 2591–2594.
10. (a) Devin, P.; Fensterbank, L.; Malacria, M. *J. Org. Chem.* **1998**, *63*, 6764–6765.
11. Lacôte, E.; Malacria, M. *C.R. Acad. Sci. Paris, Ser. IIc* **1998**, *1*, 191–194.
12. (a) Lacôte, E.; Delouvrié, B.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2116–2118; (b) Delouvrié, B.; Fensterbank, L.; Lacôte, E.; Malacria, M. *J. Am. Chem. Soc.* **1999**, *121*, 11395–11401.
13. Imboden, C.; Villar, F.; Renaud, P. *Org. Lett.* **1999**, *1*, 873–875.
14. Bogen, S.; Gulea, M.; Fensterbank, L.; Malacria, M. *J. Org. Chem.* **1999**, *64*, 4920–4925.
15. (a) Leca, D.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4220–4222; (b) Leca, D.; Song, K.; Albert, M.; Grangeio Gonçalves, M.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Synthesis* **2005**, 1405–1420.
16. Ouvry, G.; Quiclet-Sire, B.; Zard, S. Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 5002–5006.
17. (a) Kim, S.; Cho, C. H.; Lim, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9574–9575; (b) Cho, C. H.; Kim, S. *Can. J. Chem.* **2005**, *83*, 917–921; Phosphonoiminyl radicals can fragment to give nitriles. See Quiclet-Sire, B.; Zard, S. Z.; Zhang, H. *J. Organomet. Chem.* **2002**, *643–644*, 404–408.
18. Clive, D. L. J.; Kang, S. *J. Org. Chem.* **2001**, *66*, 6083–6091.
19. (a) Ingold, K. U.; Roberts, B. P. *Free-radical Substitution Reactions*; Wiley-Interscience: New York, NY, 1971; (b) Ingold, K. U.; Walton, J. C. *Acc. Chem. Res.* **1986**, *19*, 72–77; (c) Schiesser, C. H.; Wild, L. M. *Tetrahedron* **1996**, *52*, 13265–13314; (d) Walton, J. C. *Acc. Chem. Res.* **1998**, *31*, 99–107; (e) Crich, D. *Helv. Chim. Acta* **2006**, *89*, 2167–2182.
20. Coulomb, J.; Certal, V.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 633–637.
21. For recent reviews, see: (a) Leca, D.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Chem. Soc. Rev.* **2005**, *34*, 858–865; (b) Marque, S.; Tordo, P. *Top. Curr. Chem.* **2005**, *250*, 43–76.
22. (a) Bentrude, W. G. *Acc. Chem. Res.* **1982**, *15*, 117–123; (b) Bentrude, W. G. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; Wiley: Chichester, UK, 1990; Vol. 1, p 531.
23. (a) Stacey, F. W.; Harris, J. F. *Org. React.* **1963**, *13*, 150–376; (b) Walling, C.; Pearson, M. S. *Top. Phosphorus Chem.* **1966**, *3*, 1–56; (c) Herpin, T. F.; Motherwell, W. B.; Roberts, B. P.; Roland, S.; Weibel, J.-M. *Tetrahedron* **1997**, *53*, 15085–15100; (d) Deprèle, S.; Montchamp, J.-L. *J. Org. Chem.* **2001**, *66*, 6745–6755; (e) Jessop, C. M.; Parsons, A. F.; Routledge, A.; Irvine, D. *Tetrahedron Lett.* **2003**, *44*, 479–483; (f) Jessop, C. M.; Parsons, A. F.; Routledge, A.; Irvine, D. J. *Tetrahedron: Asymmetry* **2003**, *14*, 2849–2851; (g) Lopin, C.; Gouhier, G.; Gautier, A.; Piettre, S. R. *J. Org. Chem.* **2003**, *68*, 9916–9923; (h) Gautier, A.; Garipova, G.; Salcedo, C.; Balieu, S.; Piettre, S. R. *Angew. Chem., Int. Ed.* **2004**, *43*, 5963–5967; (i) Beaufils, F.; Dénès, F.; Renaud, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 5273–5275; (j) Mimeau, D.; Delacroix, O.; Gaumont, A.-C. *Chem. Commun.* **2003**, 2928–2929; (k) Mu, X.-J.; Zou, J.-P.; Qian, Q.-F.; Zhang, W. *Org. Lett.* **2006**, *8*, 5291–5293; (l) Hirai, T.; Han, L.-B. *Org. Lett.* **2007**, *9*, 53–55.
24. (a) Crich, D.; Hao, X. *J. Org. Chem.* **1996**, *61*, 3566–3570; (b) Crich, D.; Hao, X. *J. Org. Chem.* **1997**, *62*, 5982–5988; (c) Crich, D.; Yao, Q. *Tetrahedron* **1998**, *54*, 305–318; (d) Crich, D.; Yao, Q. *Org. Lett.* **2003**, *5*, 2189–2191; (e) Crich, D.; Yao, Q. *J. Am. Chem. Soc.* **2004**, *126*, 8232–8236; For other applications of homolytic substitutions of thioesters, see: (f) Benati, L.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Strazzari, S.; Zanardi, G. *Org. Lett.* **2002**, *4*, 3079–3081; (g) Hayes, C. J.; Herbert, N. M. A.; Harrington-Frost, N. M.; Pattenden, G. *Org. Biomol. Chem.* **2005**, *3*, 316–327; (h) De Boeck, B.; Harrington-Frost, N. M.; Pattenden, G. *Org. Biomol. Chem.* **2005**, *3*, 340–347.
25. (a) Benati, L.; Calestani, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Strazzari, S. *Org. Lett.* **2003**, *5*, 1313–1316; (b) Benati, L.; Bencivenni, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Scialpi, R.; Spagnolo, P.; Zanardi, G. *J. Org. Chem.* **2006**, *71*, 3192–3197; (c) Bencivenni, G.; Lanza, T.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Zanardi, G. *Org. Lett.* **2008**, *10*, 1127–1130.
26. (a) Wada, T.; Kondoh, A.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, *10*, 1155–1157; (b) Shirai, T.; Kawaguchi, S.; Nomoto, A.; Ogawa, A. *Tetrahedron Lett.* **2008**, *49*, 4043–4046; For an early example using organometallic catalysis, see: (c) Han, L. B.; Tanaka, M. *Chem. Lett.* **1999**, 863–864.
27. Serra, A. C.; da Silva Corrêa, C. M. M. *Tetrahedron Lett.* **1991**, *32*, 6653–6654.
28. One of the referees suggested an alternative mechanism featuring an atom transfer process initiated by *S*-radical cyclization, followed by sulfonylation from the S.M. This mechanism appears unlikely since sulfonylation would arise from homolytic substitution at the S(VI) atom of a thiosulfonate. Crich has shown that homolytic substitutions of sulfones were highly unlikely processes, and this is probably also the case for thiosulfonates. See: Crich, D.; Hutton, T. K.; Ranganathan, K. *J. Org. Chem.* **2005**, *70*, 7672–7678.
29. Craig, D. C.; Durie, A.; Edwards, G. L.; Sinclair, D. J. *Tetrahedron Lett.* **1995**, *36*, 1307–1310.
30. Edwards, G. L.; Muldoon, C. A.; Sinclair, D. J. *Tetrahedron* **1996**, *52*, 7779–7788.
31. For general reviews on sulfur-centered radicals including reactivity of sulfonyl radical toward alkynes, see: (a) Chatgilialoglu, C.; Bertrand, M. P.; Ferreri, C. In *S-Centered Radicals*; Alfassi, Z. B., Ed.; Wiley: New York, NY, 1999; Chapter 11; (b) Bertrand, M. P.; Ferreri, C. In *Radicals in Organic Synthesis*, 1st ed.; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, Chapter 5.5.
32. Wolfe, J. P.; Rennels, R. A.; Buchwald, S. L. *Tetrahedron* **1996**, *52*, 7525–7546.
33. Bundy, G. L.; Lin, C. H.; Sih, J. C. *Tetrahedron* **1981**, *37*, 4419–4429.
34. Jones, D. N.; Hill, D. R.; Lewton, D. A.; Sheppard, C. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1574–1587.
35. (a) Hall, C. D.; Lowther, N.; Tweedy, B. R.; Hall, A. C.; Shaw, G. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2047–2054; (b) Stockland, R. A., Jr.; Taylor, R. I.; Thompson, L. E.; Patel, P. B. *Org. Lett.* **2005**, *7*, 851–853.
36. Semenzin, D.; Etemad-Moghadam, G.; Albouy, D.; Diallo, O.; Koenig, M. *J. Org. Chem.* **1997**, *62*, 2414–2422.
37. Pudovik, A. N.; Batyeva, E. S. *Zh. Obshch. Khim.* **1969**, *39*, 334–337.
38. Griffin, C. E.; Kundu, S. K. *J. Org. Chem.* **1969**, *34*, 1532–1539.