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The Iodine Atom Transfer Addition Reaction (I-ATRA) Initiated by AIBN: Optimization, Scope and Radical Reaction Pathways

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ABSTRACT: *Optimization of reaction conditions (alkene, halide, solvent, stoichiometry, manners of the reagents addition, and reaction time) of the I-ATRA reactions involving 1-iodoalkylphosphonates was carried out. GC–MS–CI/EI analyses showed main and side products of this reaction and the corresponding radical reaction pathways leading to products derived from phosphorus and nonphosphorus containing iodides, as well as explained the source of hydrogen in radical reduction processes accompanying the I-ATRA reaction. Synthesis of some 3-iodoalkyl and 3-iodoalkenylphosphonates was also presented based on the optimized procedure.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:22–35, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20187

INTRODUCTION

In recent years in our laboratory, we have investigated addition reactions of phosphonate radicals derived from various 1-, 2-, or 3-heterosubstituted phosphonates **1** to alkenes and alkynes under reductive [1] and atom transfer (nonreductive) reaction conditions (I-ATRA) [2,3] (Scheme 1). The latter reaction leading to 3-iodoalkyl and 3-iodoalkenylphosphonates **2** was for the first time carried out by us with AIBN as the radical initiator and was a subject of recent mechanistic investigations [3–6]. Preliminary synthetic results were also presented [2].

In this publication, we would like to perform our comprehensive investigations concerning optimization of reaction conditions as well as a scope and limitations of the I-ATRA reaction, mainly involving 1-iodoalkylphosphonates [7]. In this aspect, very helpful were detailed GC–MS–CI/EI analyses of various reaction mixtures showing formation of main and all side products of this reaction as well as the corresponding radical reaction pathways both for phosphorus and nonphosphorus containing iodides. Synthesis of some 3-iodoalkyl and 3-iodoalkenylphosphonates is also contained.

RESULTS AND DISCUSSON

Optimization of the I-ATRA Reaction Conditions

Starting Halides. In a series of diethyl 1-haloalkylphosphonates, only 1-iodoalkylphosphonates gave with 1-hexene and AIBN as the radical initiator, the I-ATRA products of type **2** in satisfactory 74–100% yields (Table 1).

Neither chlorine nor bromine atoms were efficiently transferred in the X-ATRA reactions

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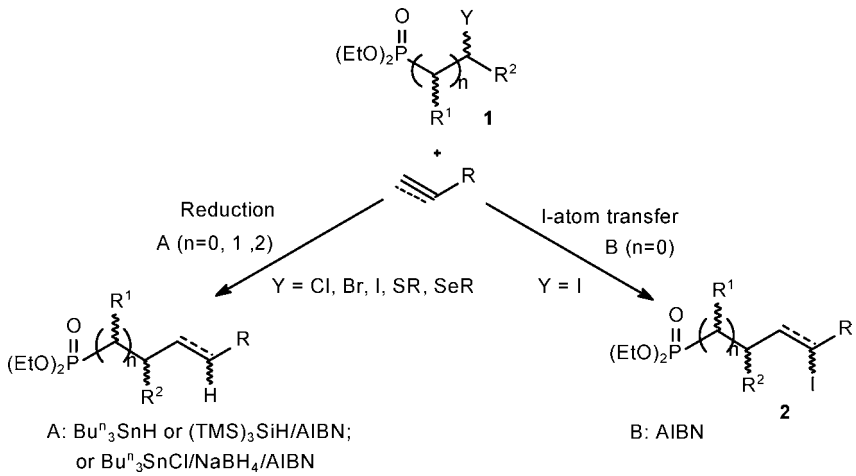
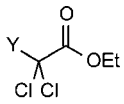
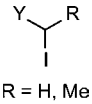


SCHEME 1 Formation of functionalized phosphonates under A: reductive and B: atom transfer reaction conditions.

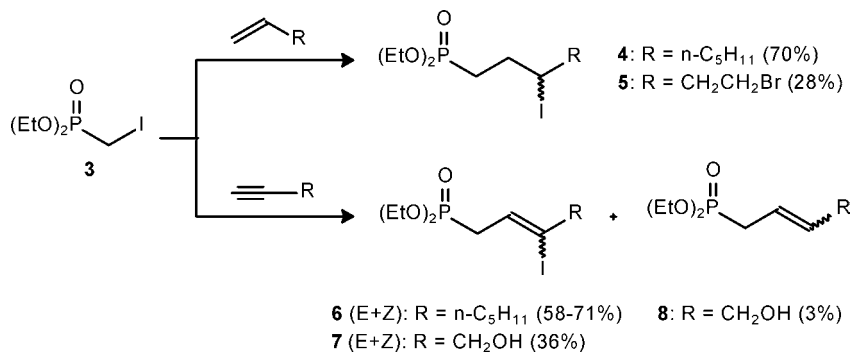
TABLE 1 The Reaction of 1-Haloalkylphosphonates with 1-Hexene Initiated by AIBN

Phosphonate					 R = H, Me
Yield of product **2** 0 ($n = 0$, $R^2 = H$, R = Bu^n) with 1-hexene (%)	0	10	13	74–100	

Y = (EtO)$_2$P(O).

(X = Cl, Br). In the reactions of 1-bromobenzylphosphonate and dichlorophosphonoacetate, only traces of corresponding products of type **2** with 1-hexene were detected based on ^{31}P-NMR (Table 1). Therefore, in our further investigations, we used only organic iodides with which we obtained the corresponding I-ATRA products. Alkyl, phenyl, and allyl iodides gave other types of products (GC–MS investigations, vide infra). In contrast to the described PhSe group transfer reaction (PhSe-GTRA) [8], neither MeS nor PhS groups could be transferred from diethyl 1-sulfenyl-2-oxoalkylphosphonates to alkenes under the same reaction conditions.

Starting Alkenes. Excellent reactivity showed terminally unsubstituted alkenes (for instance, 1-hexene and 1-hexadecene) and alkynes (1-heptyne) [2]. A somewhat inferior yields were obtained with terminally unsubstituted alkenes modified by heteroatoms (allyl and propargyl alcohols, homoallyl bromide) due to the competitive reduction of starting iodides (see also GC–MS investigations, Scheme 2, and Experimental). No reaction occurred with 1-*O*, 1-*S*, and 1-*N*-substituted alkenes and diethyl 1-iodomethylphosphonate (*n*-butyl vinyl ether—as a solvent in 20-fold excess; phenyl vinyl sulfide—10 eq., benzene, 5 h and 1-vinyl-2-pyrrolidinone—10 eq., benzene, 7 h). In contrast to homoallyl bromide, allyl bromide turned out to be unreactive (MS–CI investigations, vide infra). Sterically hindered 1,2-disubstituted alkenes (cyclopentene—in excess as a



SCHEME 2 Synthesis of 3-iodoalkyl- and 3-iodoalkenylphosphonates in the I-ATRA reactions.

TABLE 2 Yields of the I-ATRA Phosphonate Products in Various Solvents

Time (h)	*$(EtO)_2P(O)(CH_2)_2CH(I)$-Bu^n (%)*	*$(EtO)_2P(O)CH_3$ (%)*	*$(EtO)_2P(O)CH_2I$ (%)*
	$CHCl_3$		
4	58	6	36
9.5	68	8	24
14.5	67	8	24
	$ClCH_2CH_2Cl$		
5	55	13	12
7	~ 50	14	10
	C_6H_6		
7	71–83	0–8	17–20
	1-Hexene		
7	76	7	17

solvent, in $CHCl_3$ or in C_6H_6, 5 h; cyclohexene—in benzene, 18 h), and 2,2-disubstituted alkenes [(+)-limonene—as a solvent or in benzene, 5 h; (−)-camphene in benzene] were also unreactive (vide infra). Methyl acrylate was polymerized in the presence of stoichiometric amount of AIBN (benzene, 9 h) before the iodine atom transfer process could occur.

Solvent. Generally, I-ATRA reactions can be carried out in a variety of solvents (benzene, chloroform, 1,2-dichloroethane, PEG-400, and anisole); however, the best yields of 74–100% were obtained in benzene. For instance, in the tested reaction of diethyl iodomethylphosphonate with 1-hexene (10 eq.) in the presence of AIBN (1 eq.), the corresponding I-ATRA product **2** ($n = 0$, $R^2 = H$, $R = Bu^n$) was obtained in up to 83% yield while in chloroform the yield was lowered to 68% (Table 2). Some small amount of diethyl iodomethylphosphonate and the starting iodide were also detected.

Very good yields were also obtained in low boiling 1-alkenes as solvents, which could be easily evaporated after the reaction. To our surprise, toluene and mesitylene gave the corresponding I-ATRA product in 29 and 0% yields, respectively, while in anisole the yield was similar to that obtained in toluene (28%).

Stoichiometry. Optimized reaction conditions required the use of 10 eq. of lower boiling alkenes (like 1-hexene). In the case of higher boiling alkenes (like 1-hexadecene), at least 5 eq. of an alkene per 1 eq. of the starting iodide was sufficient. In a general procedure, AIBN was usually used in equimolar amount with reference to the starting iodide as for lower boiling alkenes. In some cases 0.5–1 eq. of AIBN also gave satisfactory but a somewhat inferior yields. Catalytic amount (up to 20%) of AIBN significantly lowered the yield to 33%. A sequential addition of AIBN allowed us to maintaining lower amounts of the initiator which gave reasonable yields of the I-ATRA product **2** ($n = 0$, $R^2 = H$, $R = Bu^n$); however, reaction times had to be increased four to ten times depending on volatility of alkene (Table 3, vide infra).

Manners of the Reagents Addition. Usually, the syringe pump technique is used for a slow addition of reagents to maintain a low concentration of radicals. In the I-ATRA reactions of low reactive 1-iodoalkylphosphonates, concentration of radicals was sufficiently low; therefore, the initiator and all reagents could be dissolved in a solvent in a single

TABLE 3 Yields of Products **2** in a Sequential Addition of AIBN

AIBN (%)	*$(EtO)_2P(O)(CH_2)_2CH(I)$-Bu^n (%)*	*$(EtO)_2P(O)CH_3$ (%)*	*$(EtO)_2P(O)CH_2I$ (%)*	*Time (h)*
5	17	3	79	5
10	42	5	51	13
15	39	6	51	19
20	44	8	45	24.5
25	45	9	45	36.5
30	52	12	32	45
35	52	13	30	50
40	58	14	24	55.5
AIBN (%)	*$(EtO)_2P(O)(CH_2)_2CH(I)(CH_2)_{13}CH_3$ (%)*	*$(EtO)_2P(O)CH_3$ (%)*	*$(EtO)_2P(O)CH_2I$ (%)*	*Time (h)*
5	29	4	63	8
15	42	9	42	14
20	46	11	27	19.5
25	57	12	15	26.5

addition procedure and refluxed for 6–9 h. The syringe pump technique did not improved yields and gave even a somewhat inferior results (65% versus 71–83% without the pump, in benzene).

We also investigated a sequential addition of AIBN in the reaction of diethyl iodomethylphosphonate with 1-hexene in benzene (Table 3).

The corresponding I-ATRA product **2** ($n = 0$, $R^2 = H$, $R = Bu^n$) was obtained in 58% yield using sequentially 40% molar amount of AIBN within a very long reaction time of 55.5 h. The same 58% yield of the product was gained upon a single addition of almost the same 50% molar amount of AIBN within 6 h only (i.e. 10 times shorter). When 1-hexene was replaced by the higher boiling 1-hexadecene, the above 57% yield of the product **2** ($n = 0$, $R^2 = H$, $R = (CH_2)_{13}CH_3$) was obtained even with lesser 25% molar amount of AIBN, within 26.5 h in a sequential procedure (Table 3). The identical 57% conversion was obtained with 20% amount of AIBN within 6 h (i.e. four times shorter) in a single addition procedure.

Reaction Time. Usually, 6–9 h was an optimum reaction time to obtain the best yields of the I-ATRA products. Prolongation of the reaction time over 9 h did not increased yields of I-ATRA products (Table 2).

Synthesis of 3-Iodoalkyl- and 3-Iodoalkenylphosphonates

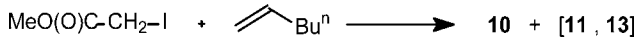
Based on the elaborated, optimized procedure, we synthesized a few new functionalized phosphonates **4–8** using the I-ATRA reaction (Scheme 2). Good yields of **4** (70%) were obtained for 1-heptene; however, for some heterosubstituted alkenes (4-bromobut-1-ene) and alkynes (propargyl alcohol), large amount of the starting diethyl iodomethylphosphonate remained unreacted in the reaction mixture and therefore lower yields of the corresponding products **5** and **7** (28–36% based on ^{31}P-NMR) were obtained. However, the starting material could be regenerated during separation of the I-ATRA products with the column chromatography over silica gel increasing the yields to 58–69%. Trace amount of the reduced product **8** was detected and separated when propargyl alcohol was used (see Experimental, GC–MS investigations). We were also successful in chromatographic separation of the *E*/*Z* mixture of **7**. Similar moderate yields gave allyl alcohol regardless of the reaction time (7–14 h) and scale: 41% of the product as a *E*/*Z* mixture in a 2.5–3.5/1 ratio ($\delta^{31}P$ = 31.9/31.2 ppm, benzene) and 43% of the starting diethyl iodomethylphosphonate. Additional portion of AIBN (10%) added after the first 7 h in refluxing benzene, in order to convert the remaining substrate to the product and a simultaneous prolongation of the reaction time to 14 h, did not increased the yield.

On the other hand, good yields were obtained for terminally unsubstituted alkynes, such as 1-heptyne (58–71% of **6** depending on the reaction scale, the lower yield was obtained for a bigger reaction scale). In this reaction, 22–31% of the starting diethyl iodomethylphosphonate remained unreacted and 6–11% of diethyl methylphosphonate was additionally formed. The starting iodomethylphosphonate could be regenerated, but an attempt to convert it quantitatively to **6** with additional (30%) amount of AIBN again did not changed the ratio of signals in ^{31}P-NMR spectra. The phosphonate **6** was obtained as a mixture of *E*/*Z* regioisomers in a ratio 1.7–2.2/1 depending on the reaction scale (2.2/1 for a bigger scale, 6 h). Since unequivocal assignment of configuration of **6** *E*/*Z* could not be done based on the additive increments method, we assumed a bigger shielding effect of the iodine atom in comparison to the alkyl groups. Thus, in **6E**, the PCH_2 group being close to the n-C_5H_{11} moiety was deshielded (δ_H = 2.75 ppm versus 2.57 ppm in **6Z**) while the vinylic proton was shielded by the iodine atom (δ_H = 5.57 ppm versus 6.18 ppm in **6Z**). Other nonphosphorus products accompanying **6–8** are disclosed in Schemes 9 and 10.

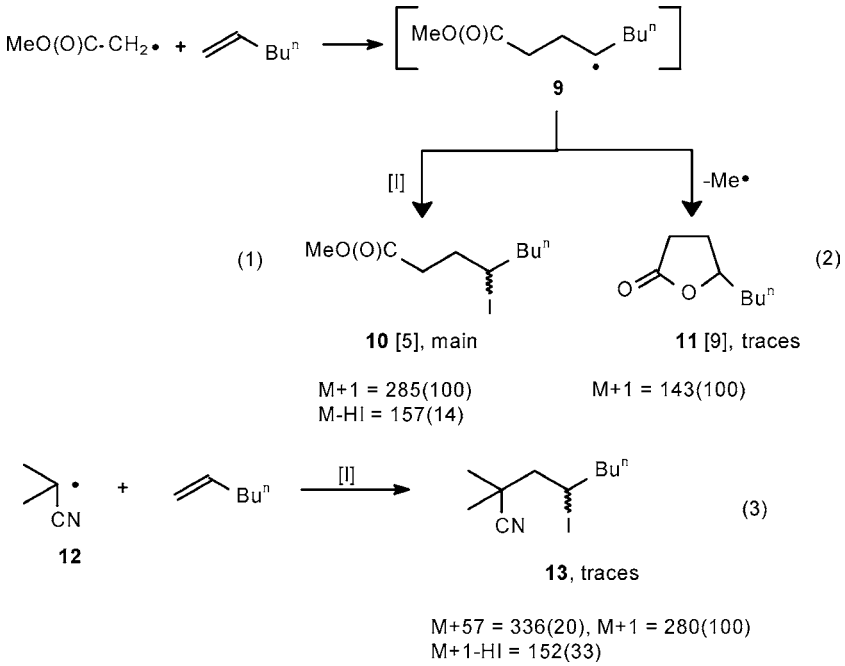
Investigation of Radical Reaction Pathways in the I-ATRA Reaction with the GC–MS–CI/EI Techniques

This part of the work shows the results of investigations of the I-ATRA reaction pathways involving iodides of differentiated reactivities (from very reactive to unreactive) and unsaturated substrates having substituents of various stereoelectronic properties. Main products were isolated and fully characterized. Side products formed in trace quantities could be characterized only with MS–CI/EI techniques. All known compounds **10, 11, 17, 22b, 30, 46, 48–50** have been referred in the literature.

Reaction of Methyl Iodoacetate with 1-Hexene (a Very Reactive Iodide)



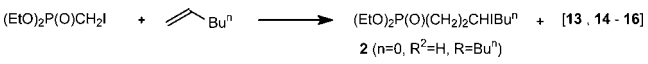
According to our earlier studies on the competitive reactions [5], methyl iodoacetate belongs to the most reactive iodides in the intermolecular I-ATRA reactions initiated by AIBN. The main reaction pathway



SCHEME 3 Formation of main and side products in the I-ATRA reaction of methyl iodoacetate with 1-hexene.

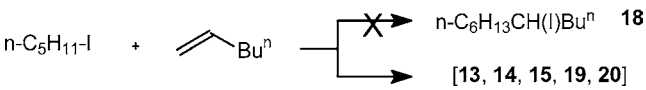
led to the expected product **10** (Eq. (1), Scheme 3). Side pathways were not developed; only traces of products **11** and **13** were formed (Eqs. (2) and (3), Scheme 3). This experiment shows that (a) practically, lack of side products in this reaction is connected with high reactivity of iodoacetate (compare with iodomethylphosphonate below), (b) the ratio of the I-ATRA products **10**/**13** is determined by the speed of the faster transfer process, and (c) the use of stoichiometric amount of AIBN does not influence the amount of **13** formed.

Reaction of Diethyl Iodomethylphosphonate with 1-Hexene (a Low Reactive Iodide)



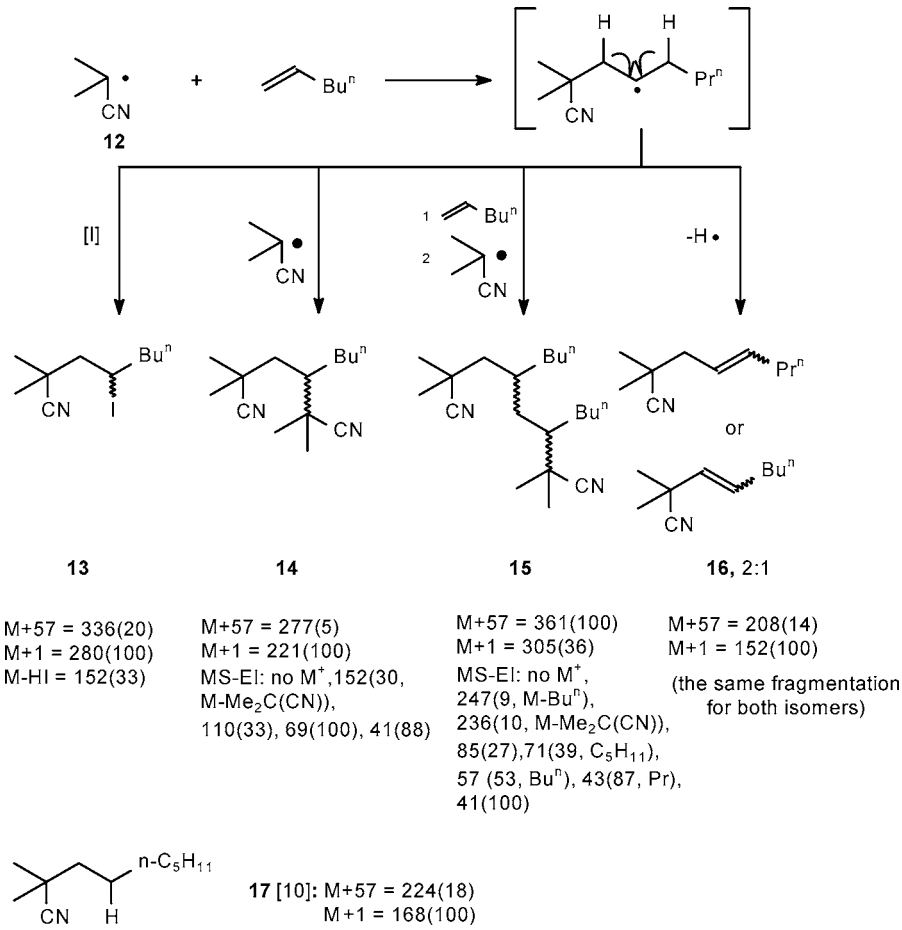
This phosphonate iodide belongs to a group of iodides possessing a lower reactivity in the intermolecular I-ATRA reactions (two to three orders of magnitude in comparison to $NC\text{-}CH_2I$, $MeO(O)CCH_2I$, or $ArC(O)CH_2I$) [5]. In this case other mechanistic pathways began to compete, which led to the formation of increasing number of side products **13, 14–16** (Scheme 4). In spite of this, the corresponding I-ATRA product, i.e. diethyl 3-iodo-*n*-heptylphosphonate **2** ($n = 0$, $R^2 = H$, $R = Bu^n$), was obtained in good yield (74–83%). In addition, in this reaction two minor compounds, i.e. diethyl methylphosphonate (0–10%) and tetraethylethylenephosphonate (0–2%), were also formed as termination reaction products [3]. For the analogous reaction carried out with 1-heptene, the reduction product **17** was additionally detected (not found in the case of 1-hexene) (Scheme 4).

Reaction of n-Amyl Iodide with 1-Hexene



This experiment was carried out in order to compare reactivity of electrophilic phosphonate radical (vide supra) with reactivity of nucleophilic *n*-amyl radical in the reaction with 1-hexene.

In this reaction, the following three main products were formed instead of the expected I-ATRA product **18**: the dimer of **12** ($M = 136$), another iodine atom transfer product **13** ($M = 279$), and the complex product **15**. Other products **14, 19**, and **20** were formed in trace quantities (Scheme 5). All formed products were formed as a result of the isobutyronitrile radical **12**, and the *n*-amyl radical **21** (derived from *n*-amyl iodide) attacks onto 1-hexene (Schemes 5 and 6). In the latter case, however, the competitive elimination of hydrogen occurred rather than the I-ATRA reaction to give undec-4-ene **22b** (Scheme 6). In the GC–MS/EI

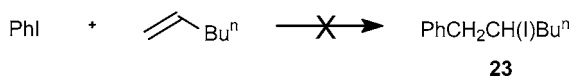


SCHEME 4 Formation of products **13, 14–17** in the reaction resulting from isobutyronitrile radical **12** attack onto 1-hexene in the reaction of this alkene with diethyl iodomethylphosphonate and AIBN.

(DB-17 column) spectra, this compound showed characteristic C_3H_7 [43(100)], C_4H_9 [57(80)], C_5H_1 [71(26)], and $C_5H_{11}CH_2$[85(20)] fragments. The presence of the latter excluded formation of the second regioisomer, i.e. undec-5-ene **22a**.

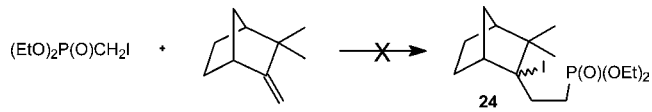
Analysis of MS–CI and MS–EI spectra of the complex compound **15** possessing the parent peak at $m/z = 304$ led to a proposition of the unsymmetrical structure (Scheme 4) and excluded formation of the symmetrical dimer derived from the dimerization of the corresponding adduct radical. In this case, in the MS–EI spectrum, a signal at $m/z = 152$ of high intensity, due to the preferential, symmetrical C—C bond cleavage of the hypothetical dimer, was not present.

Reaction of Iodobenzene with 1-Hexene (the Iodide of the Lowest Reactivity)

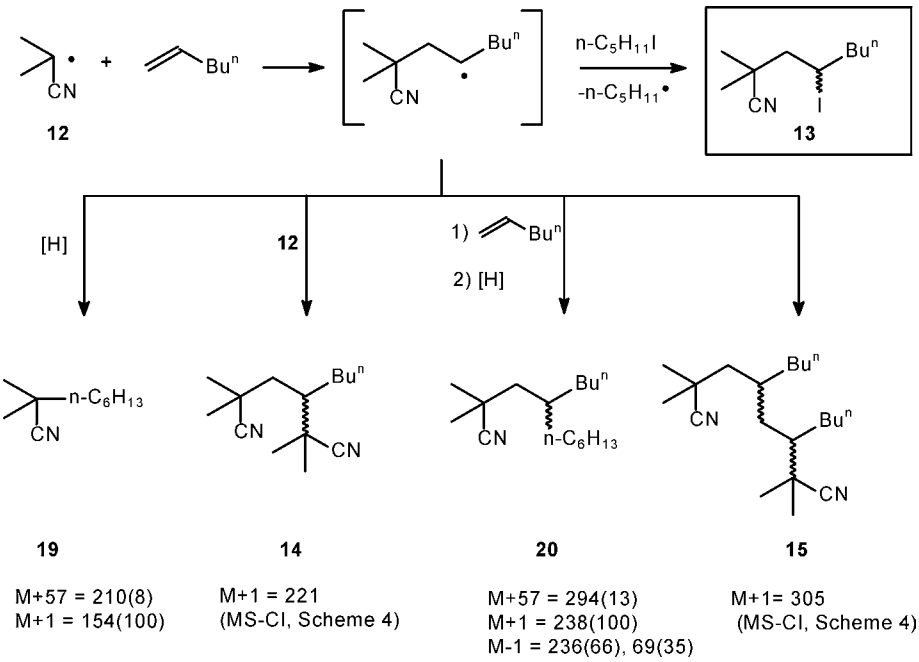


Due to the lack of stabilization of phenyl radical derived from iodobenzene, the I-ATRA product **23** was not detected both in GC–MS–CI and ^{1}H-NMR spectra (lack of characteristic —CHI signals). Other pathways involving reactions of **12** dominated to give the same side products as in the reactions of diethyl iodomethylphosphonate with 1-hexene and 1-heptene (Scheme 4). Additionally, the adduct **20** was detected in the reaction mixture.

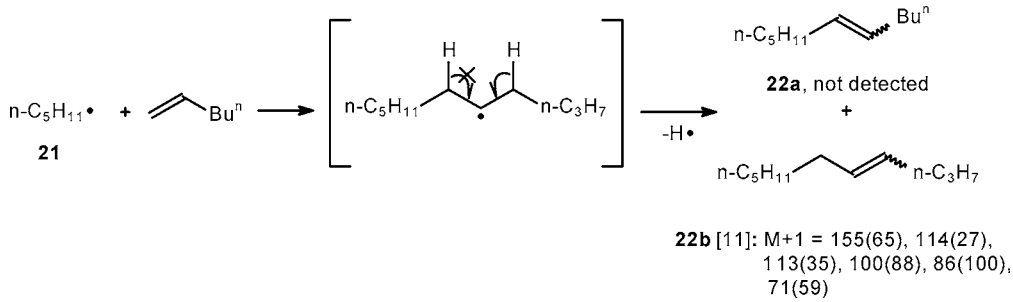
Reaction of Diethyl Iodomethylphosphonate with (−)-Camphene (2,2-Disubstituted Alkene as the Radical Acceptor)



According to ^{31}P-NMR spectrum of the crude reaction mixture, the expected I-transfer product **24**



SCHEME 5 Formation of products **14, 15, 19, 20** in the reaction resulting from isobutyronitrile radical **12** attack onto 1-hexene in the reaction of this alkene with *n*-amyl iodide and AIBN.

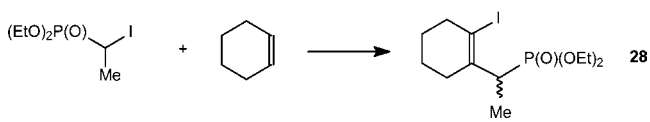


SCHEME 6 Formation of the compound **22b** in the reaction resulting from *n*-amyl radical attack onto 1-hexene in the reaction of this alkene with *n*-amyl iodide and AIBN.

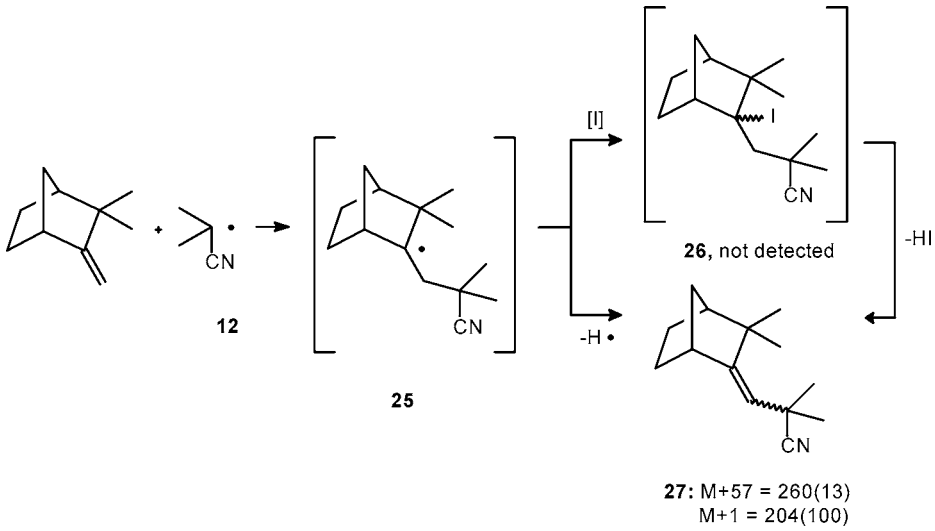
was formed in 3% yield only ($\delta^{31}P = 34.06$ ppm), most probably due to a large steric hindrance in the iodine atom transfer stage involving the crowded tertiary adduct radical **25** [6]. This minor product accompanied the starting iodomethylphosphonate (97%). The side reaction pathway involved the isobutyronitrile radical **12** attack onto (−)-camphene with the final formation of the new alkenic product **27** either via (a) iodine atom transfer to give **26** followed by the spontaneous HI elimination or (b) by a direct hydrogen elimination (Scheme 7).

Thus, this experiment shows that 2,2-disubstituted alkenes are practically unreactive in the I-ATRA reaction.

Reaction of Diethyl 1-Iodoethylphosphonate with Cyclohexene (1,2-Disubstituted Alkene as the Radical Acceptor)



1,2-Disubstituted alkenes (cyclohexene and cyclopentene) turned out to be susceptible to steric hindrance as did 2,2-disubstituted ones (96% recovery of the starting iodoalkylphosphonate). Side processes A and B, however, led to the formation of nonphosphorus containing modified cycloalkene **30** either via the

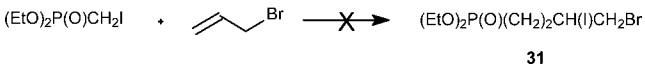


SCHEME 7 Formation of the alkenic compound **27** resulting from isobutyronitrile radical **12** attack onto (–)-camphene in the reaction of this alkene with diethyl iodomethylphosphonate and AIBN.

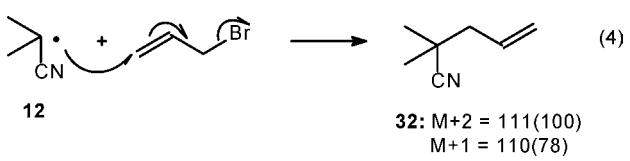
HI elimination from the I-ATRA product **29** (pathway A) or via direct elimination of hydrogen from the corresponding adduct radical to give **30** (pathway B) (Scheme 8).

In contrast to the reaction with (–)-camphene (vide supra), both products, i.e. iodocycloalkane **29** and cycloalkene **30**, were formed in a ratio of 1:3 in favor of the alkene. The possible domination of the pathway B over the propagation pathway A can also, in addition to steric reasons, constitute an explanation for the lack of progress in the whole reaction leading to **28**.

Reaction of Diethyl Iodomethylphosphonate with Allyl Bromide (Allyl Halide as the Radical Acceptor)



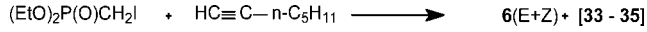
In contrast to homoallyl bromide [2], allyl bromide did not produced the I-ATRA product **31** due to operation of the dominating pathway involving the isobutyronitrile radical **12** attack onto allyl bromide to give **32**. The resulting product **32** could also be derived from a recombination of the radical **12** with the propenyl radical, formed from allyl bromide.



(4)

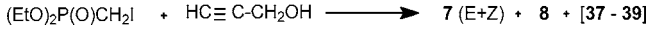
The only accompanying products were unreacted iodomethylphosphonate and the dimer of **12**.

Reaction of Diethyl Iodomethylphosphonate with 1-Heptyne



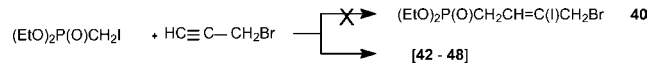
The main I-ATRA product **6** of the described reaction (vide supra) was obtained as a *E*/*Z* mixture (see also Experimental). Among nonphosphorus-containing products, **33–35** were found as a result of the I-ATRA process and hydrogen elimination reaction (Scheme 9).

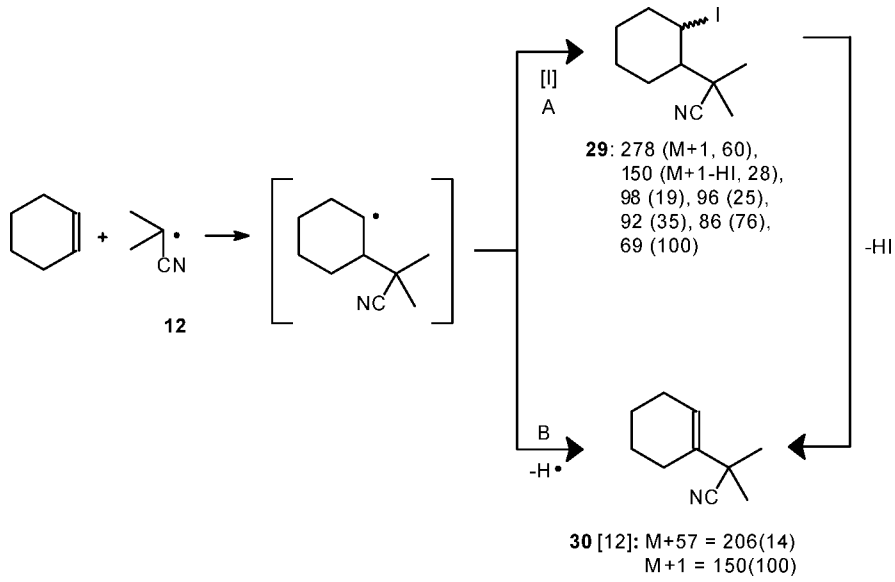
Reaction of Diethyl Iodomethylphosphonate with Propargyl Alcohol



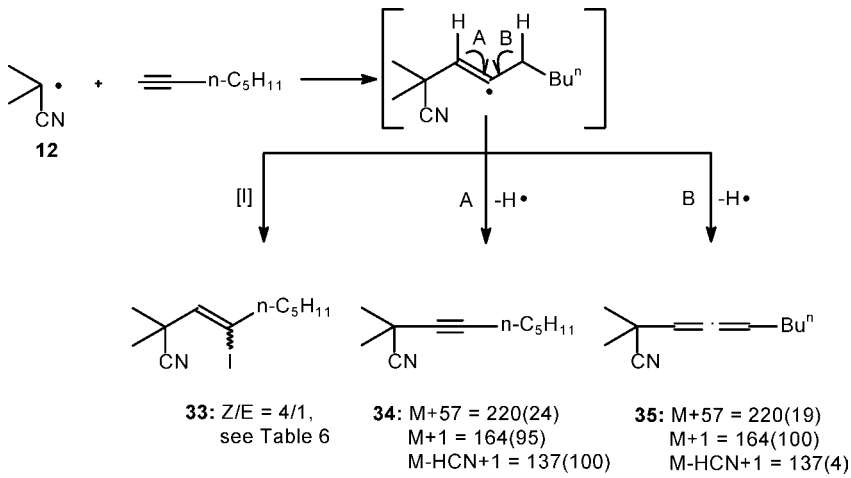
In the described reaction with nonprotected propargyl alcohol (vide supra), the I-ATRA products **7** (*E*/*Z* = 3.6/1) and **8** accompanied formation of easily separated nonphosphorus-containing mixture of **37–39** (Scheme 10). They constitute disproportionation products of the intermediate alkenyl radical **36**.

Reaction of Diethyl Iodomethylphosphonate with Propargyl Bromide





SCHEME 8 Formation of compounds **29** and **30** resulting from isobutyronitrile radical **12** attack onto cyclohexene in the reaction of this alkene with diethyl 1-iodoethylphosphonate and AIBN.

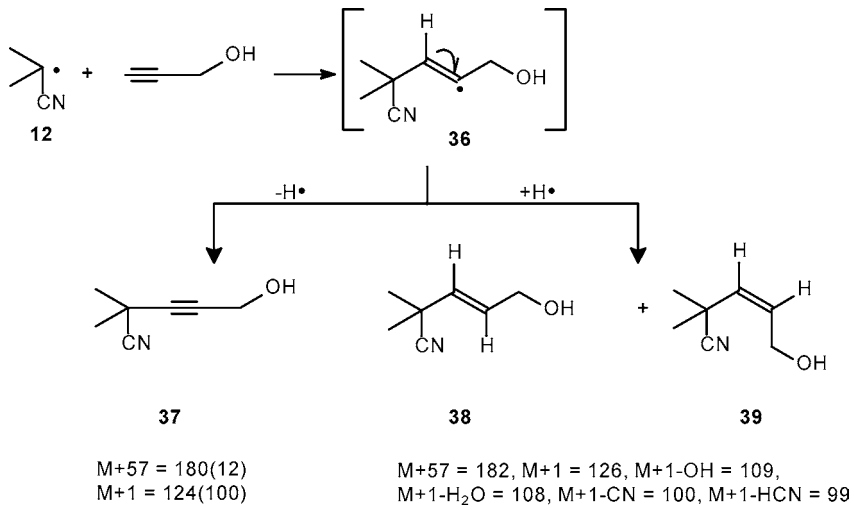


SCHEME 9 Formation of compounds **33–35** resulting from isobutyronitrile radical **12** attack onto 1-heptyne in the reaction of this alkyne with diethyl iodomethylphosphonate and AIBN.

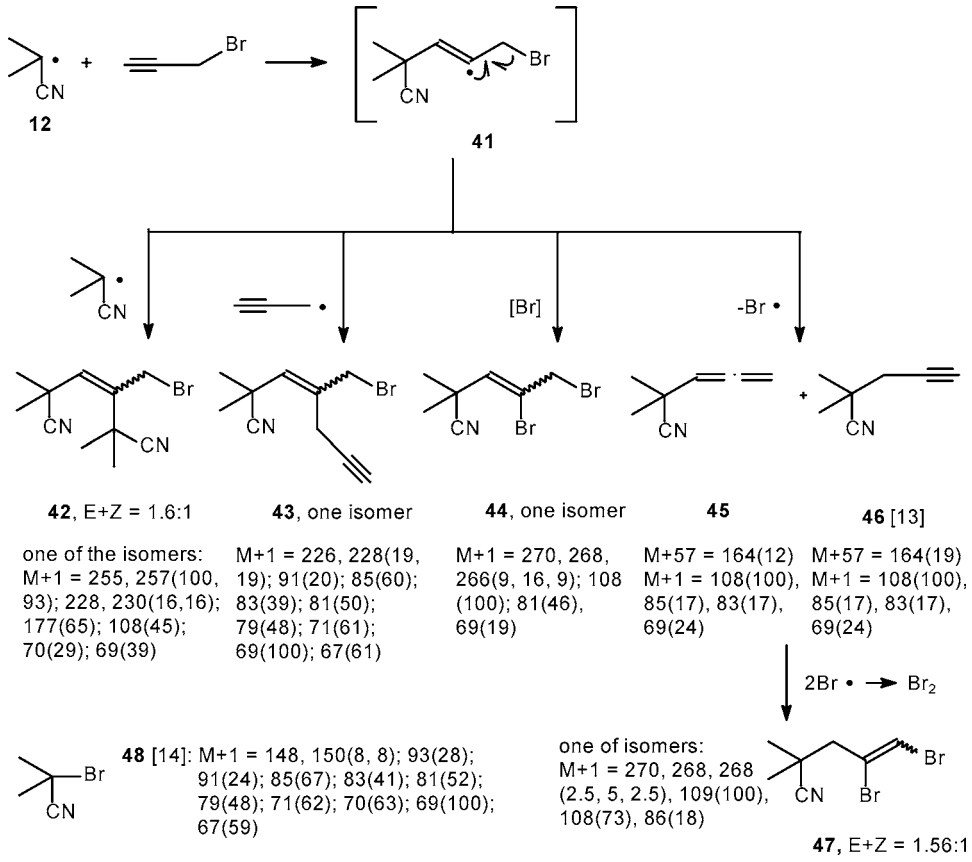
This reaction was carried out in order to compare reactivities of propargyl bromide with allyl bromide (Eq. (4)) and other triple bond containing substrates (propargyl alcohol and 1-heptyne) (Scheme 11).

It turned out that similarly to the reaction with allyl bromide, the phosphonate I-ATRA product **40** was not formed. Instead, two recombination products **42** and **43**, the bromination product **44**, and two elimination products **45** and **46** derived from the adduct radical **41** were detected. From **46**, a mixture of **47** $E + Z$ was formed via the bromine addition. Moreover, the isobutyronitrile radical attack onto bromine of propargyl bromide led to the formation of propynyl radicals and 2-bromo-2-methylpropionitrile **48** [14]. Propynyl radicals could also be formed in reactions of any C-radical present in the reaction mixture with excess of propargyl bromide.

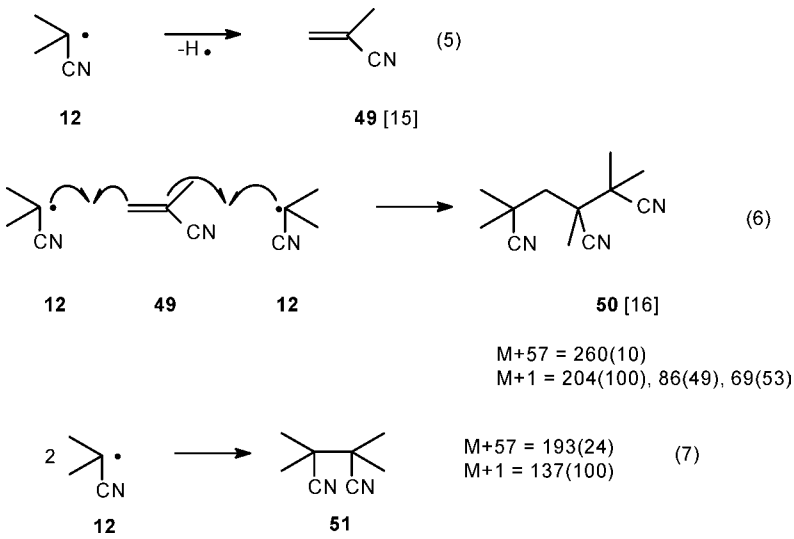
In all reactions, independently of the iodide [$(EtO)_2P(O)CH_2I$, $(EtO)_2P(O)CH(Me)I$, PhI, etc.], alkene (1-hexene, 1-heptene, allyl bromide etc.), or alkyne (1-heptyne, propargyl alcohol) used, there were three unidentified signals detected in GC–MS spectra (DB-17 column) at the following retention



SCHEME 10 Formation of compounds **37–39** resulting from isobutyronitrile radical **12** attack onto propargyl alcohol in the reaction of this alkyne with diethyl iodomethylphosphonate and AIBN.



SCHEME 11 Formation of compounds **42–48** resulting from isobutyronitrile radical **12** attack onto propargyl bromide in the reaction of this alkyne with diethyl iodomethylphosphonate and AIBN.



SCHEME 12 Reactions of the radical **12**, leading to combination products **50** and **51**.

times: 7′39″ [M + 1 = 94(100), 93(59), 92(22)]; 9′65″ [M + 1 = 108(100), 107(84), 106(39), 69(20)], and 22′71″ [M + 57 = 260(10), M + 1 = 204(100), 86(49), 69(53)]. At least in the latter case, one can speculate that due to the big concentration of isobutyronitrile radicals **12**, the mass $m/z = 203$ belongs to the species **50** resulting from the possible attack of **12** onto methacrylonitrile **49** followed by a combination of the formed adduct radical with the second radical **12** (Scheme 12, Eqs. (5) and (6)). The former reaction leading to **49** may be a source of hydrogen in the minor reductive processes observed in the I-ATRA reactions, leading to **8, 17, 19, 20**. The reduction products may be alternatively formed as a result of attack of **12** onto methyl hydrogen of AIBN which leads to decomposition of the latter. Due to the use of AIBN as the radical initiator, in each I-ATRA reaction, easily separable tetramethylsuccinodinitrile **51** was formed as one of main reaction products (Scheme 12, Eq. (7)).

In summary, in this paper, we performed comprehensive studies on radical reaction pathways in the I-ATRA reaction involving various organic iodides and alkenes or alkynes. In particular, we (1) detected all reaction products in crude reaction mixtures of several model reactions involving various substrates of differentiated reactivity; (2) showed all possible intermediates and reaction pathways leading to main and side products; (3) showed scope and limitations of the investigated reaction explaining, based on the MS results, why some reagents (organic iodide and/or unsaturated compound) are unreactive in the sense of the iodine atom transfer. In particular, it concerned a comparison of large reactivity of terminally unsubstituted alkenes with the lack of reactivity in the case of 1,2- and 2,2-disubstituted alkenes; (4) carried out investigations showing the influence of several factors on the course of the new reaction, such as structure of iodide and unsaturated compounds, temperature, solvent, reaction time, stoichiometry, and manners of the reagents addition; (5) explained the source of hydrogen in radical reduction processes accompanying the I-ATRA reactions. Overall, the presented results allow better understanding of the iodine atom transfer reaction initiated by AIBN, and now it will enable broader applications of this useful reaction in organic synthesis.

EXPERIMENTAL

General

The ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded using a Bruker AC-200 spectrometer. The IR spectra were recorded using an ATI Mattson Infinity FTIR 60 spectrometer. The mass spectra of pure compounds were obtained using a Finnigan Mat 95 spectrometer.

The MS–CI spectra of the crude reaction mixtures were recorded with the GC–MS hyphenated technique using 30 m DB-17 column and a 50°C(5)-250°C(10), 10°C/min program. The reaction of methyl iodoacetate with 1-hexene and the reaction of diethyl iodomethylphosphonate with propargyl alcohol were analyzed with 30-m DB-1 column using the same program. Measurements were carried out twice for the same sample: (a) before evaporation

of the solvent (C_6H_6) in order to detect low boiling products and (b) after evaporation of the solvent for a check up. The GC–MS–EI spectra of the crude reaction mixtures were recorded under the same reaction conditions as for the GC–MS–CI technique.

Column chromatography was done using Merck silica gel (F_{254} 60, 70–230 and 270–400 mesh). Organic solvents were purified by standard procedures. Alkenes and alkynes used were of commercial purity. Organic iodides were prepared according to the following literature references.

Diethyl iodomethylphosphonate [3,17,18], yield = 75%, ^{31}P-NMR: $\delta = 20.5$ ppm ($CDCl_3$). Diethyl 1-iodoethylphosphonate [3], yield = 71%, ^{31}P-NMR: $\delta = 23.5$ ppm ($CDCl_3$). Diethyl benzylphosphonate [19], yield = 90%, ^{31}P-NMR: $\delta = 26.9$ ppm ($CDCl_3$). Diethyl 1-chloroethylphosphonate [20,21], yield = 56%, ^{31}P-NMR: $\delta = 21.6$ ppm ($CDCl_3$). Diethyl 1-chlorobenzylphosphonate [21], yield = 62%, ^{31}P-NMR: $\delta = 18.1$ ppm ($CDCl_3$). Diethyl 1-bromobenzylphosphonate was obtained via bromination of 1-hydroxybenzylphosphonate with (a) Ph_3P/CBr_4 system [22] (8 h reflux, $n_D^{23} = 1.5299$,^{31}P-NMR: $\delta = 17.6$ ppm ($CDCl_3$), yield = 38%); (b) $SOBr_2$ (CH_2Cl_2, 25°C, 1 day, 27% yield, a new procedure). Diethyl 1,1-dichloro-2-oxo-*n*-butylphosphonate [22], yield = 80%, ^{31}P-NMR: $\delta = 8.76$ ppm ($CDCl_3$).

Other nonphosphorus-containing iodides like *n*-amyl, phenyl, and allyl were commercially available.

The following iodine atom transfer products **4–8** were synthesized by mixing all substrates and AIBN in benzene and refluxing for 7–9 h according to the described general procedure [2,3].

Diethyl 3-Iodo-n-octylphosphonate **4**

Reagents and solvents used were diethyl iodomethylphosphonate (5 mmol, 1.39 g), 1-heptene (50 mmol), AIBN (5 mmol, 820 mg), and benzene (70 mL). The crude product obtained as oil was purified on preparative TLC plates using a mixture of solvents: petroleum ether/acetone = 2:1. Yield 70% (1.32 g).

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 0.88 (t, 3H, $^3J_{H,H} = 6.5$ Hz, C^8H_3), 1.32 [t, 6H,$^3J_{H,H} = 7.1$ Hz, $(CH_3CH_2O)_2P$], 1.24–2.09 (m, 12H, PCH_2CH_2, $C^4H_2(CH_2)_2C^7H_2$), 4.09 (m, 5H, $(CH_3CH_2O)_2P$, CHI) ppm. ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 3.96 (s, C^8H_2), 16.39 (d, $^3J_{C,P} = 5.5$ Hz, CH_3CH_2OP), 22.43 (s, C^7H2); 26.07 (d, $^1J_{C,P}$ = 141.26, CP), 29.07 (s, C^6H_2), 30.91 (s, C^5H_2), 33.42 (d, $^2J_{C,P} = 3.2$, C^2H_2), 39.38 (d, $^3J_{C,P}$ = 19.25 Hz, CHI), 40.33 (s, C^4H_2), 61.65 (d, $^2J_{C,P}$ = 6.4 Hz, CH_3CH_2OP) ppm. ^{31}P-NMR (81 MHz, $CDCl_3$): $\delta = 31.26$ ppm. IR (film): υ (cm^{-1}) 2979, 2956, 2929, 2871, 2836, 1467, 1437, 1391, 1366, 1096, 1056, 1030, 964, 788, 530; MS–CI (isobutane): *m/z* (%) 377 ($M^+ + 1$, 100), 249 (73); MS–EI (70 eV): (%) 249 ($M^+ - I$, 100), 137 (11); MS–HR–CI: $M^+ + 1$, found: 377.07227; $C_{12}H_{27}O_3PI$ requires *m/z* 377.07425.

Diethyl 5-Bromo-3-iodo-n-pentylphosphonate **5**

Reagents and solvents used were diethyl iodomethylphosphonate (1.8 mmol, 500 mg), 4-bromobut-1-ene (18 mmol, 1.83 mL), AIBN (1.8 mmol, 295 mg), and benzene (10 mL). The crude product obtained as oil was purified with a column chromatography over silica gel (Merck 60, 230–400 mesh) using a gradient of solvents: petroleum ether/acetone (from 4 to 43% of acetone). The separation was not complete, and fractions of the highest concentration of the product were purified again with preparative TLC plates using a mixture of solvents: benzene: ethyl acetate = 1:1. Yields: 28% (crude, based on ^{31}P-NMR)/20% (149 mg, isolated)/58% (after regeneration of diethyl iodomethylophosphonate).

^{1}H-NMR (500 MHz, $CDCl_3$): $\delta = 1.33$ [t, 6H, $^3J_{H,H} = 7.1$ Hz, $(CH_3CH_2O)_2P$], 1.80–1.95 (m, 1H, PCH_2), 2.00–2.20 (m, 3H, PCH_2, PCH_2CH_2), 2.20–2.35 (m, 2H, CH_2CH_2Br), 3.53–3.62 (m, 2H, CH_2Br), 4.03–4.17 [m, 4H, $(CH_3CH_2O)_2P$], 4.17–4.26 (m, 1H, CHI) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): $\delta = 16.45$ [d, $^3J_{C,P} = 6.0$ Hz, $(CH_3CH_2O)_2P$], 24.03 (d, $^1J_{C,P} = 142.7$ Hz, PCH_2), 30.82 (d, $^5J_{C,P} = 4.5$ Hz, CH_2Br), 31.96 (d, $^2J_{C,P} = 3.7$ Hz, PCH_2CH_2), 41.20 (s, CH_2CH_2Br), 54.77 (d, $^3J_{C,P} = 21.2$, CHI), 61.72 (d, $^2J_{C,P} = 5.2$ Hz, CH_3CH_2OP), 61.76 (d, $^2J_{C,P} = 5.9$ Hz, CH_3CH_2OP) ppm. ^{31}P-NMR (81 MHz, $CDCl_3$): δ = 0.67 ppm. IR (film): υ (cm^{-1}) 3453, 2980, 2906, 1731, 1433, 1392, 1257, 1164, 1097, 1061, 1018, 964, 800; MS–CI (isobutane): *m/z* (%) 415 ($M^+ + 1$ (^{81}Br), 87), 413 ($M^+ + 1$ (^{79}Br), 100), 367 (21), 287 (35), 285 (25), 154 (44); MS–EI (70 eV): *m/z* (%) 414 (M^+ (^{81}Br), 0.5), 412 (M^+ (^{79}Br), 0.5), 287 (70), 285 (70), 152 (29), 149(100), 67 (45); MS–HR–CI: $M^+ + 1$, found: 412.93428; $C_9H_{20}O_3PBrI$ requires 412.93590.

Diethyl 3-Iodooct-2-enylphosphonate **6**

Oil, *E*/*Z* = 1.7–2.2/1, yield: 58–71%; ^{1}H-NMR (200 MHz, $CDCl_3$): $\delta = 0.89$ (m, 2 × 3H, C^8H_3, $E + Z$), 1.32 [t, 2 × 3H, $^3J_{H,H} = 7.1$ Hz, (CH_3CH_2O, $E + Z$)], 1.15–1.65 (m, 2 × 6H, $C^5H_2C^6H_2C^7H_2$, $E + Z$), 2.37 (td, 2H, $^3J_{H,H} = 7.3$ Hz, $^5J_{H,P} = 2.5$ Hz, C^4H_2, Z), 2.50 (m, 2H, $^3J_{H,H} = 7.0$ Hz, $^5J_{H,P} = 3.6$, C^4H_2, *E*), 2.57 (dd, 2H, $^2J_{H,P} = 21.8$ Hz, $^3J_{H,H} = 8.0$ Hz, C^1H_2, *Z*), 2.75 (dd, 2H,$^2J_{H,P} = 21.9$, $^3J_{H,H} = 7.3$ Hz, C^1H_2, *E*), 4.11 (dq,

$2 \times 4H$, $^3J_{H,P} = 7.2$ Hz, $^3J_{H,H} = 7.2$ Hz, CH_3CH_2O, *E* + *Z*), 5.57 (td, 1H, $^3J_{H,H} = 7.3$ Hz, $^3J_{H,P} = 6.9$ Hz, C^2H, *E*), 6.18 (td, 1H, $^3J_{H,H} = 8.0$ Hz, $^3J_{H,P} = 6.9$ Hz, C^2H, *Z*) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$) : $\delta = 3.91$ (s, C^8H_3), 16.39 (d, $^3J_{C,P} = 5.9$ Hz, CH_3CH_2O), 22.28, 22.42 (s, C^7H_2), 28.70, 28.85, 30.19, 30.53 (s, $C^5H_2C^6H_2$), 28.99 (d, $^1J_{C,P} = 141.4$, C^1H_2), 35.01 (d, $^1J_{C,P} = 139.9$, C^1H_2), 38.47, 45.20 (s, C^4H_2), 62.00 (d, $^2J_{C,P} = 6.5$ Hz, CH_2O), 62.06 (d, $^2J_{C,P} = 8.6$ Hz, CH_2O), 107.51 (d, $^3J_{C,P} = 18.2$ Hz, C^3I), 114.51 (d, $^3J_{C,P} = 18.1$ Hz, C^3I); 124.38 (d, $^2J_{C,P} = 9.8$ Hz, C^2H), 128.63 (d, $^2J_{C,P} = 10.4$ Hz, C^2H) ppm. ^{31}P-NMR (81 MHz, $CDCl_3$): $\delta = 5.13$ (*Z*), 26.70 (*E*) ppm. IR (film): υ (cm^{-1}) 3474 (broad), 2979, 2957, 2931, 2863, 2860, 1645, 1458, 1392, 1254, 1222, 1164, 1098, 1054, 1029, 965, 798, 727, 518; MS–CI (isobutane): *m/z* (%) 375 ($M^+ + 1$, 100), 247 ($M^+ + 1 - HI$, 18); MS–EI (70 eV): *m/z* (%) 247 ($M^+ - I$, 100), 191 (20), 109 (26); MS–HR–CI: $M^+ + 1$, found: 375.05725; $C_{12}H_{25}O_3$ PI requires 375.05860.

Diethyl 4-Hydroxy-3-iodobut-2-enylphosphonate **7E, 7Z**

Reagents and solvents used were diethyl iodomethylophosphonate (1.248 mmol, 347 mg), 2-propyn-1-ol (12.5 mmol, 737 μL), AIBN (1.248 mmol, 205 mg), and benzene (9 mL). The crude product (*E*/*Z* = 1.5:1) obtained as oil was purified first with column chromatography and then with preparative TLC plates using a gradient of solvents: *n*-hexane:acetone. Yields: 36% (crude based on ^{31}P-NMR)/29% (121 mg, isolated)/69% (after regeneration of diethyl iodomethylophosphonate).

7*E*: ^{1}H-NMR (200 MHz, $CDCl_3$): $\delta = 1.33$ (t, 6H, $^3J_{H,H} = 7.1$ Hz, $POCH_2CH_3$), 2.79 (ddt, 2H, $^2J_{H,P} = 22.0$ Hz, $^3J_{H,H} = 7.5$ Hz, $^5J_{H,H} = 1.1$ Hz, PCH_2), 3.00 (br s, 1H, O*H*), 3.95–4.20 (m, 4H, $POCH_2CH_3$), 4.28 (m, 2H, CH_2OH), 6.02 (tdt, 1H, $^3J_{H,H} = 7.5$ Hz, $^3J_{H,P} = 6.7$ Hz, $^4J_{H,H} = 1.5$ Hz, *H*—C═C) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): $\delta = 6.45$ (d, $^3J_{C,P} = 6.0$ Hz, CH_3CH_2OP), 34.31 (d, $^1J_{C,P} = 139.7$ Hz, PCH_2), 62.28 (d, $^2J_{C,P} = 6.6$, CH_3CH_2OP), 71.39 (s, CH_2OH), 113.02 (s, HC═CI), 125.21 (d, $^2J_{C,P} = 9.7$ Hz, HC═CI) ppm. ^{31}P-NMR (81 MHz, $CDCl_3$): $\delta = 26.18$ ppm. IR (film): ν (cm^{-1}) 3347, 2982, 2928, 2909, 2854, 1728, 1644, 1443, 1393, 1242, 1164, 1081, 1046, 1025, 968, 800, 716, 663, 545; MS–CI (isobutane): *m/z* (%) 335 ($M^+ + 1$); MS–EI (70 eV): *m/z* (%) 207 ($M^+ - I$, 72), 133 (100); MS–HR–CI: $M^+ + 1$, found 334.99071; $C_8H_{17}O_4PI$ requires 334.99092.

7*Z*: ^{1}H-NMR (200 MHz, $CDCl_3$): $\delta = 1.33$ (t, 6H, $^3J_{H,H} = 7.1$ Hz, $POCH_2CH_3$), 1.70 (br s, 1H, O*H*), 2.73 (dd, 2H, $^2J_{H,P} = 22.5$ Hz, $^3J_{H,H} = 8.5$ Hz, PCH_2), 3.95–4.20 (m, 4H, $POCH_2CH_3$), 4.36 (s, 2H, CH_2OH), 6.26 (td, 1H, $^3J_{H,H} = 8.5$ Hz, $^3J_{H,P}$= 6.4) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): $\delta = 16.45$ (d, $^3J_{C,P} = 5.7$, CH_3), 28.82 (d, $^1J_{C,P} = 138.5$, PCH_2), 62.82 (d, $^2J_{C,P} = 7.1$ Hz, CH_3CH_2OP), 67.71 (d, $^4J_{C,P} = 2.5$ Hz, CH_2OH), 107.21 (d, $^3J_{C,P} = 15.5$ Hz, HC═CI), 129.47 (d, $^2J_{C,P} = 12.3$ Hz, HC═CI) ppm. ^{31}P-NMR (81 MHz, $CDCl_3$): $\delta = 25.66$ ppm. IR (film): υ (cm^{-1}) 3360, 2963, 2922, 2852, 1444, 1394, 1369, 1260, 1162, 1029, 973, 801; MS–CI (isobutane): *m/z* (%) 335 ($M^+ + 1$); MS– EI (70 eV): *m/z* (%) 207 ($M^+ - I$, 81), 161 (23), 133 (100); MS–HR–CI: $M^+ + 1$, found 334.99192; $C_8H_{17}O_4PI$ requires 334.99092.

Diethyl 4-Hydroxy-but-2-enylphosphonate **8**

Only one stereoisomer was isolated as an oily substance (3% based on ^{31}P-NMR) from the reaction mixture. ^{1}H-NMR (200 MHz, $CDCl_3$): $\delta = 1.32$ (t, 6H, $^3J_{H,H} = 7.0$ Hz, $POCH_2CH_3$), 2.30 (broad s, 1H, CH_2OH), 2.60 (dd, 2H, $^2J_{H,P} = 21.7$ Hz, $^3J_{H,H} = 6.3$ Hz, $P(O)CH_2$), 3.95–4.40 (m, 6H, $POCH_2CH_3$, CH_2OH), 5.50–6.15 (m, 2H, CH═CH) ppm. ^{31}P-NMR (81 MHz, $CDCl_3$): $\delta = 27.77$ ppm. MS–CI (isobutane): *m/z* (%) 209 ($M^+ + 1$, 100), 191 (67); MS–HR–CI: $M^+ + 1$, found: 209.09393; $C_8H_{18}O_4P$ requires 209.09427.

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