Iodine atom transfer addition reaction of 1-iodoalkyl phosphonates to alkenes in the presence of α,α′-azoisobutyronitrile (AIBN): mechanistic aspects†‡

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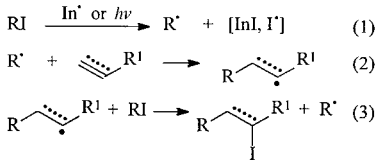
The objectives of this work were to elucidate the mechanistic pathway of the title reaction, which constitutes the first example of a radical iodine atom transfer addition reaction of non-fluorine-containing phosphonates, and to determine whether 2-iodo-2-methylpropionitrile, **8**, can serve as a competing iodine donor with the starting diethyl 1-iodoalkyl phosphonates, **1a**,**b**. The title reaction was found to proceed with AIBN as the sole radical initiator, not requiring poisonous tin reagents as co-initiators, and gave diethyl 3-iodoalkylphosphonates **3a**–**e** (the final products of the propagation step, isolated in 59–95% yield), tetramethylsuccinodinitrile, **9**, diethyl methylphosphonate, **4** and tetraethyl ethylenebisphosphonate **5** (all termination products, 0–10% yields). The radical character of this reaction was demonstrated using TEMPO as a radical trap. **8** (the intermediate of the initiation step), synthesized independently from AIBN and iodine, caused complete inhibition of the reaction when added to the reaction mixture, indicating that it does not behave as an iodine donor in the transfer stage, but rather as an inhibitor.

Atom or group transfer radical reactions, particularly easy in the case of organic iodides, have recently joined fundamental methods for the formation of carbon–carbon bonds in both organic synthesis[2] and polymer chemistry.[3] The commonly accepted mechanism (Scheme 1) of these reactions comprises three basic steps: generation of the substrate radical, either photolytically or thermally [eqn. (1)], addition of the latter to a multiple bond [eqn. (2)] and the appropriate iodine atom transfer step[4–7] [eqn. (3)].

The driving force behind iodine atom transfer reactions is the formation of a more stable starting radical in comparison to a less stable adduct radical. Moreover, the latter reactions must be faster than other competing reactions of the adduct radical, such as telomerization or termination.[2] The mechanisms of the iodine atom transfer reactions have been investigated mostly for iodides that do not contain additional heteroatoms geminal to the transferred iodine atom.

Recently, we have begun a sustained program that is designed to exploit the characteristic features of novel reactions involving 1-diethoxyphosphorylalkan-1-, 2- and 3-yl radicals as new, reactive intermediates and their applications in organic synthesis. In a series of papers[8–15] we have demonstrated the considerable synthetic value of the tributyltin hydride-mediated reactions [Scheme 2, eqn. (1)].

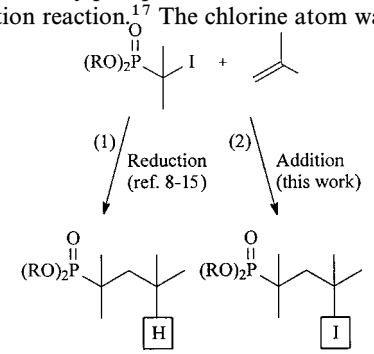


Scheme 1 A general mechanism for the iodine atom transfer addition reaction of non-phosphorus-containing iodides to alkenes and alkynes.

† Electronic supplementary information (ESI) available: ^{13}C DEPT and 2D ^{1}H–^{13}C correlation spectra for **3a**,**c**–**e**. See http://www.rsc.org/suppdata/nj/b0/b005882n/

‡ Part VIII of the series *Phosphorus containing radicals*. For part VII, see: ref. 1.

Now, we extend our interest to the iodine atom transfer addition reactions, which certainly possess a greater synthetic value due to the possible further synthetic transformations of the iodine atom in the product [Scheme 2, eqn. (2)]. The mechanisms of these reactions have not been broadly investigated due to the limited number of reported cases. According to the Beilstein Crossfire database, there are only two examples of the iodine atom transfer reaction reported in the literature, involving diethyl iododifluoromethylphosphonate[16] and diethyl iodofluoromethylphosphonate.[17] For these reactions, performed in the presence of Cu(0) or $Pd(PPh_3)_4$, a single electron transfer, radical mechanism was proposed. In our hands the use of these initiators failed for non-fluorine-containing phosphonates. However, we succeeded in carrying out, for the first time, the iodine atom transfer addition reaction with α,α′-azoisobutyronitrile (AIBN) as the sole reaction initiator without it being necessary to use poisonous tin reagents like $(n\text{-}Bu_3Sn)_2$ or $n\text{-}Bu_3SnH$ as co-initiators. The results concerning the mechanism of this reaction are disclosed in this paper. It is also noteworthy that transfer reactions of other halogen atoms *via* radical-type mechanisms are also represented in the literature by a very limited number of examples. The bromine atom was transferred from diethyl bromodifluoromethylphosphonate onto olefins in a free radical addition reaction.[17] The chlorine atom was transferred



Scheme 2 Free radical addition reaction under reductive and atom transfer reaction conditions.

from diethyl trichloromethylphosphonate onto olefins in reactions initiated by CuCl/amine[18] and $FeCl_3$ or $CuCl_2/Et_3N \cdot HCl$/benzoin systems.[19] While the latter reaction proceeds *via* a redox chain, the former is a nonchain catalytic reaction. The above examples show that different reaction mechanisms operate for the halogen atom transfer reactions in α-hetero (Cl, Br, I) substituted phosphonates, depending on the structure of the starting phosphonates and the mode of the initiation step.

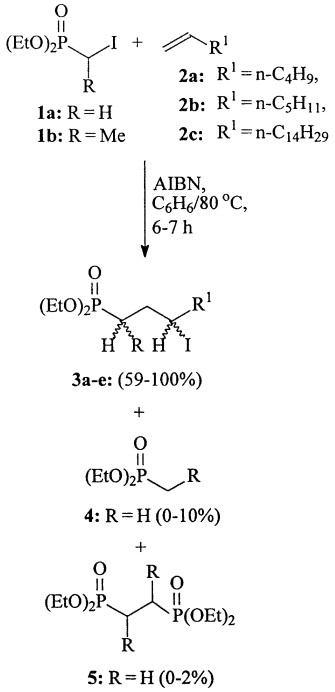
Results and discussion

Optimization of the reaction conditions and characterization of the reaction products

It is known from the literature that the efficiency of iodine atom transfer reactions carried out for non-phosphorus-containing substrates, in the presence of AIBN as the sole reaction initiator, varies with the structure of the reactants. For instance, the reaction of electrophilic 1-iodoperfluoropropane with electron-rich 1-heptene gave perfluoropropyl-2-iodoheptane in 99% yield (1% AIBN, 6 h, 70 °C).[20] On the other hand, the similar addition reaction of propargyl iodomalonates with 1-hexene resulted in only 15% conversion and cyclization of iodoalkynes in the presence of AIBN, hexa-*n*-butylditin, led to unidentified decomposition products.[4] Therefore, an accurate determination of the optimal reaction conditions was the first task in our studies. As a model reaction for the mechanistic studies, the reaction of diethyl 1-iodoalkylphosphonates **1a**,**b** with 1-hexene, **2a**, 1-heptene, **2b** and 1-hexadecene, **2c**, in refluxing benzene in the presence of AIBN was chosen, which resulted in the formation of the adducts **3a**–**e** (Scheme 3).

We found that the best results could be obtained upon mixing reagents in a ratio **1** : AIBN : **2** varying from 1 : 0.5 : 10 to 1 : 1 : 10 and heating the resulting mixture in refluxing benzene for 6 h. Under these reaction conditions the yields of the phosphonates **3a**–**e** was in the range 59–95% (see Experimental). Optimization of the reaction conditions was carried out on the synthesis of **3a**, **3c**, **3d**/**3e** and representative data for **3a** are given in Table 1.

The structure of the products **3** was confirmed not only by the MS, IR and standard ^1H-, ^{13}C-, ^{31}P-NMR but also by the



Scheme 3 The iodine atom transfer addition reaction of diethyl iodoalkylphosphonates **1** to alkenes **2**.

Table 1 Optimization of the reactant stoichiometry for the reaction of **1a** with **2a** in the presence of AIBN in C_6H_6 (80 °C, 6–7 h)

1a : AIBN : **2a**/equiv.	**3a** (%)	**1a** (%)
1 : 0 : 10	0	100
1 : 0.05 : 10	17	73
1 : 0.1 : 10	21	78
1 : 0.2 : 10	33	67
1 : 0.5 : 10	63	21
1 : 1 : 10	71–83	17–20
1 : 1 : 5	46	48
1 : 1 : 2	10	90
1 : 1 : 1	3	97

$^1H\{^{31}P\}$-, $^{13}C\{^{31}P\}$-NMR decoupled spectra. The ^{13}C-NMR (DEPT) and (^1H–^{13}C)-NMR (2D) experiments were helpful in assignment of characteristic ^1H- and ^{13}C-NMR signals to the CH_2 groups of long phosphonate chains and showed that some of these groups were diastereotopic. Moreover, the two-dimensional correlations revealed unequivocally the exact ^1H-NMR position of the CH–I multiplets that were completely hidden under the diethoxyphosphoryl methylene multiplets at around $\delta_H = 4.1$.

When the reaction was performed in the presence of a catalytic amount of AIBN (10%), the expected phosphonates **3** were formed in much lower yields. Thus, with 1-hexene, **2a**, and the higher boiling 1-heptene, **2b** and 1-hexadecene, **2c**, the 3-iodoalkylphosphonates **3a–c** were obtained in 21, 40 and 48% yield, respectively. Based on the ^1H- and ^{31}P-NMR experiments and GLC comparative analyses, the following further observations were made: (1) substrates were recovered in the absence of the radical initiator AIBN; (2) tetramethylsuccinodinitrile, **9**, as the dimerization product of isobutyronitrile radical **10**, was isolated in 80–95% yield, depending on the reaction scale (Scheme 5, *vide infra*); (3) two termination phosphorus-containing products were found in small quantities in the reaction mixture of **1a** with alkenes **2a–c**: diethyl methylphosphonate, **4** [0–10%, δ_P ($CDCl_3$) = 30.9] and tetraethyl ethylenebisphosphonate, **5** [0–2%, δ_P ($CDCl_3$) = 30.2], proving the formation of diethoxyphosphorylmethyl radicals **11** (Scheme 5, *vide infra*). In the reaction of **1b** with 1-hexene, a 1 : 1 mixture of diastereoisomers **3d** and **3e** was almost quantitatively isolated and only trace amounts of **4** were formed.

When the investigated reactions were carried out in the presence of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy radical) as the radical trap, a typical inhibitory effect was observed (regardless of the use of catalytic or stoichiometric amounts of AIBN as the radical initiator), indicating their radical character (Table 2).

Is 2-iodo-2-methylpropionitrile an iodine donor in the transfer reaction step?

In the atom transfer reactions the starting iodide usually behaves as a donor of the iodine atom [Scheme 1, eqn. (3)]. We were intrigued by the question whether 2-iodo-2-methylpropionitrile **8** [Scheme 5, *vide infra*; see also Scheme 1, eqn. (1)], can be consumed as a second competing source of the iodine atom. To the best of our knowledge, this problem was

Table 2 Reaction of **1a** with **2a** in the presence and absence of TEMPO

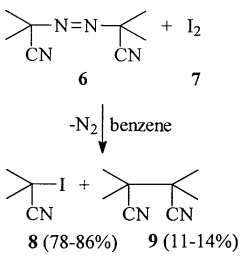
AIBN[a]/equiv.	TEMPO[a]/equiv.	Yield **3a**[b] (%)
0.1	0.1	5(30)
1	1	7(76)

[a] With respect to **1a**. [b] With TEMPO and without TEMPO (in parentheses).

not considered earlier. According to Schemes 1 and 5, **8** must be formed in the initiation step as the result of isobutyronitrile radical **10** attack on the iodine atom of the starting iodide **1**. A preliminary analysis of the ^{1}H-NMR spectra of the crude reaction mixtures showed, however, the absence of the iodide **8**, which means that it is apparently formed in trace quantities during the initiation step or is subsequently consumed in the transfer step as the iodine atom donor. We synthesized this iodide independently by the reaction of AIBN with molecular iodine (2 or 3 equiv.) in a refluxing benzene solution within 4–6 h in 78–86% yields (Scheme 4, Table 3).

Indeed, the ^{1}H-NMR spectra of the crude reaction mixtures (*i.e.* **1a** with **2a** and **2c**; **1b** with **2a**) showed no characteristic singlet at $\delta = 2.24$ ($CDCl_3$) due to the presence of the iodide **8**. Considering addition and transfer steps as rapid reactions and the fact that the iodine atom in the iodide **8** could subsequently be transferred to the adduct radical, thus shifting the equilibrium of the initiation step, we anticipated that addition of this iodide from an external source to the reaction mixture would cause higher conversions of phosphonates **1** to products. However, when reactions of **1a** with **2a** or **2c** were carried out with a stoichiometric amount of the iodide **8** (Table 4) in the presence of both catalytic or stoichiometric amounts of AIBN, only the starting 1-iodoalkylphosphonate, **1a**, the unreacted 2-iodo-2-methylpropionitrile, **8**, and AIBN and tetramethylsuccinodinitrile, **9**, could be detected in the crude reaction mixtures after 6 h.

Thus, the iodide **8** turns out not to be an iodine donor in the propagation step but an inhibitor of the initiation step, according to the Le Chatelier–Brown principle.[21] This experiment gave the additional conclusion that the initiation step has to be a reversible process and the concentrations of both resulting products, the iodide **8** and the radical **11**, are small during the reaction course, even with a stoichiometric amount of AIBN. This is consistent with the observation (^{31}P- and ^{1}H-NMR assay) of small quantities of the phosphorus termination products **4** (0–10%) and **5** (0–2%). The addition of another iodine donor, *n*-propyl iodide, used either in stoichiometric or threefold excess together with a stoichiometric amount of AIBN, to the reaction of **1a** with **2a** had, as expected, no effect, either beneficial or detrimental, and confirmed earlier conclusions for non-phosphorus substrates.[22]



Scheme 4 Independent synthesis of 2-iodo-2-methylpropionitrile, **8**, from AIBN and iodine.

Table 3 Optimization of conditions for the reaction of **6** with I_2

I_2/equiv.	**8** (%)	**9** (%)	**6** (%)
1	38	10	52
2	78	11	11
3	86	14	0

Table 4 Inhibitory effect of externally added **8** on the reaction of **1a** with **2a**

AIBN/equiv.[a]	**8**/equiv.[a]	Yield **3a** (%)[b]
1	0.1	0(21)
1	1	0(73)

[a] With respect to **1a**. [b] With **8** and without **8** (in parentheses).

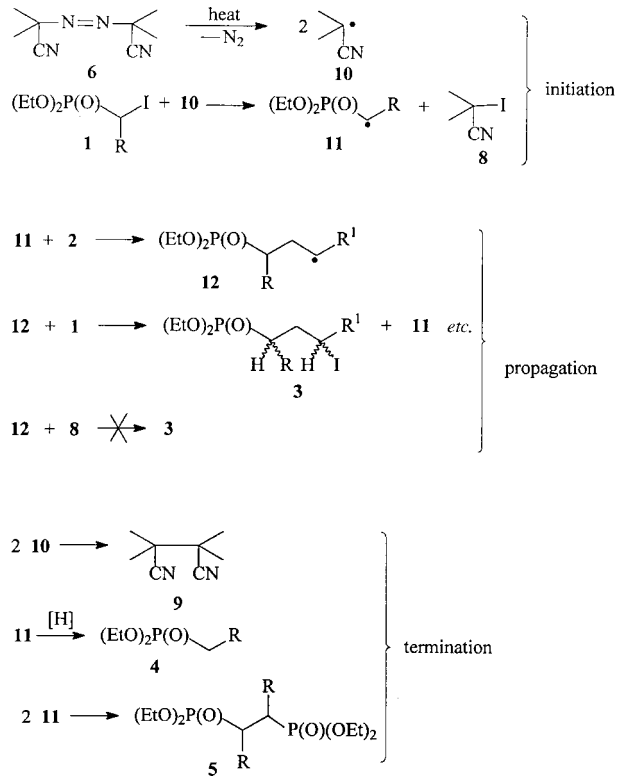
Mechanistic pathway of the iodine atom transfer addition reaction of diethyl 1-iodoalkylphosphonates to alkenes

In the radical-type mechanism postulated for the iodine atom transfer addition reaction of **1** to **2**, three main steps can be distinguished (Scheme 5).

In the first, initation step, isobutyronitrile radical **10**, generated by thermal decomposition of AIBN, reversibly reacts with the starting iodides **1** to give the key radicals **11** and the iodide **8**. Another possibility to explain the formation of **11**[23] involves the addition of isobutyronitrile radical **10** to alkenes **2**, followed by the iodine atom transfer reaction with the starting iodides **1**. However, such a route to **11** is of minor importance and does not occur to a large extent because the corresponding adducts have not been found. Moreover, the high yields of the isolated tetramethylsuccinodinitrile **9** (80–95% for the reaction of **1a** with **2c**) and of the regenerated alkenes (96% for **2c**) after column chromatography on silica gel provide convincing evidence that the radical **10** is mostly involved in the dimerization reaction leading to the dinitrile **9** rather than in the addition reaction to alkenes **2**.

In the second, propagation step, the radicals **11** undergo addition to alkenes **2** to give the adduct radicals **12**. They, in turn, are trapped by the starting iodides **1** to afford the final phosphonates **3** and radicals **11**, which are capable of reacting further with alkenes **2**. The radicals **12** are not trapped by the iodide **8**. The latter is an inhibitor of the iodine atom transfer reaction, as demonstrated above. Accumulation of the final 3-iodoalkylphosphonates **3** in the reaction mixtures is possibly due to the fact that isobutyronitrile radical **10** does not abstract an iodine atom from non-stabilized iodides. This conclusion was confirmed by the reaction of the pure phosphonate **3c** with 1-hexene, **2a**, in the presence of a stoichiometric amount of AIBN and in which only starting materials were recovered.

In the third, termination step, three reactions occur: the



Scheme 5 Mechanism of the iodine atom transfer addition reaction of diethyl iodomethylphosphonates **1** to alkenes **2** in the presence of AIBN.

dimerization of the radicals **10** and **11** to tetramethylsuccinodinitrile, **9**, and tetraethyl ethylenebisphosphonate, **5**, respectively, and the reduction of the radicals **11** to diethyl alkylphosphonates **4** (the source of hydrogen atoms is not clear).

Conclusions

In summary, in this paper we disclose the mechanistic pathway of the radical iodine atom transfer addition reaction of diethyl 1-iodoalkylphosphonates **1** to alkenes **2**, which constitutes the first example of the reaction involving non-fluorine-containing phosphonates. We confirmed the presence of all intermediate and final products of the reaction: **3**–**5**, **8** and **9** and found that this reaction may be radically initated solely with AIBN, without the necessity of using poisonous tin compounds as co-initiators. We also conclude that 2-iodo-2-methylpropionitrile, **8**, as an intermediate of the initiation step, is formed in trace quantities and for kinetic and reactivity reasons it does not compete with the starting iodide **1** as the iodine donor. This might be a general conclusion for other iodine transfer reactions involving AIBN as an initiator. The synthetic protocol presented is a general one for a radical-type synthesis of 3-iodoalkylphosphonates **3**.

Experimental

General

The ^{1}H-NMR (200 and 500 MHz), ^{13}C-NMR (50 and 125 MHz) and ^{31}P-NMR spectra (81 and 202 MHz) were recorded using Bruker AC-200 and Bruker 500 DRX spectrometers. Coupling constants (J) are given in Hz. The mass spectra were obtained using a Finnigan Mat 95 spectrometer. The IR spectra were recorded using an ATI Mattson Infinity FTIR 60 spectrometer. The preparative thin layer chromatography was performed using 20 × 20 cm Merck silica gel plates (0.5 mm) with a concentrated zone. The column chromatography was done using Merck silica gel (F_{254} 60, 70–230 and 270–400 mesh). Organic solvents were purified by standard procedures. All alkenes used were commercial reagents.

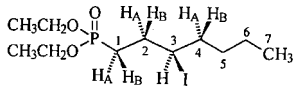
Syntheses

Diethyl iodomethylphosphonate, **1a**, was prepared according to ref. 8.

Diethyl 1-iodoethylphosphonate, 1b. To a stirred solution of diethyl ethylphosphonate (9.96 g, 0.06 mol) in THF (1 mL), the following reagents were added, at −78 °C under argon atmosphere, in 10–15 min intervals in the given order: LDA (0.066 mol), TMSCl (6.51 g, 7.61 ml, 0.06 mol), LDA (0.066 mol), iodine (15.2 g, 0.06 mol). After warming to room temperature, a EtONa–EtOH solution (prepared by dissolving 1.38 g, 0.06 mol of sodium in 30 mL ethanol) was added. Stirring was continued at this temperature for 1 h and then at 50 °C for 10 min. Next a saturated solution of ammonium chloride (50 mL) was added at room temperature and after stirring for 10 min, the THF was evaporated. To the residue H_2O (50 mL) and CH_2Cl_2 (150 mL) were added and the crude product was extracted into the organic layer, which was then washed with water (50 mL), dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was isolated using a Kugelrohr apparatus under vacuum: 87 °C/0.02 mmHg, $n_D^{24} = 1.4842$; yield 71% (purity 87% based on ^{31}P-NMR). Lit.[24] yield 83%. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.33 (t, 6H, $^3J_{H-H} = 7.1$, 2 × CH_3CH_2OP); 1.98 (dd, 3H, $^3J_{H-H} = 7.4$, $^3J_{H-P} = 17.1$, PCHCH_3); 3.84 (dq, 1H, $^3J_{H-H} = 7.4$, $^2J_{H-P} = 9.9$, P–CHI); 4.18 (dq, 4H, $^3J_{H-H} \approx {}^3J_{H-P} = 7.2$ Hz, 2 × CH_3CH_2OP); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 7.22 (d, $^1J_{C-P} = 156.06$, PCI); 16.24 (d, $^3J_{C-P} = 5.7$, $POCH_2CH_3$); 21.71 (d, $^2J_{C-P} = 3.4$, PCCH_2); 63.41 and 63.44 (2 d, $^2J_{C-P} = 3.3$ Hz, $POCH_2CH_3$); ^{31}P-NMR (202 MHz, $CDCl_3$): δ 23.54; IR (film): ν/cm^{-1} 3482 (br), 2981, 2931, 2908, 2869, 1644 (br), 1446, 1392, 1240, 1162, 1135, 1097, 1020, 966, 792, 775, 711, 561, 524; MS-LR-EI (70 eV): m/z (%) 292 (M^+, 37); 165 (36); 137 (50); 109 (100); 91 (16); 81 (29), 65 (11); MS-LR-CI (isobutane): m/z (%) 293 (MH^+, 100).

General procedure for synthesis of diethyl 3-iodoalkylphosphonates, 3a–e. To a stirred solution of diethyl 1-iodoalkylphosphonate **1a** or **1b** (5 mmol) in dry benzene (70 mL), AIBN (820 mg, 5 mmol) and the corresponding alkene **2a**, **2b** or **2c** (50 mmol) were added. The resulting solution was stirred for 10 min at room temperature and refluxed under argon atmosphere for 6–7 h. Then, benzene was evaporated and the residue was distilled using a Kugelrohr apparatus or chromatographed with silica gel. When column chromatography was employed for purification of the crude phosphonate **3c**, n-hexadecene **2c** and the starting phosphonate **1a** were regenerated in 96 and 71% yields, respectively. Tetramethylsuccinodinitrile **9** was isolated in 80–95% yield.

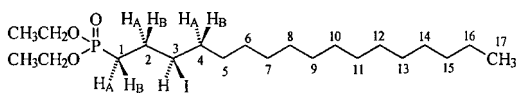
Diethyl 3-iodo-n-heptylphosphonate, ***3a***.



110 °C/0.01 mmHg; $n_D^{25} = 1.4740$; yield 74%. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.91 (t, 3H, $^3J_{H-H} = 7.1$, C^7H_3); 1.33 (t, 6H, $^3J_{H-H} = 7.1$ Hz, 2 × CH_3CH_2OP); 1.25–1.42 (m, 2H, C^5H_2); 1.45–1.57 (m, 2H, C^6H_2); 1.64–1.74 (m, 1H, C^4H^A); 1.76–1.95 (m, 2H, PCH^A, C^4H^B); 1.96–2.10 (m, 3H, PCH^B, C^2H_2); 4.06–4.18 (m, 5H, 2 × CH_3CH_2OP, CH–I); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 13.60 (s, C^7H_3); 16.24 (d, $^3J_{C-P} = 5.8$, CH_3CH_2OP); 21.63 (s, C^6H_2); 25.80 (d, $^1J_{C-P} = 141.7$, PC); 31.31 (s, C^5H_2); 33.24 (d, $^2J_{C-P} = 3.0$, C^2H_2); 39.07 (d, $^3J_{C-P} = 19.2$, C^3H–I); 39.86 (s, C^4H_2); 61.45 (2 × d, $^2J_{C-P} = 4.7$ Hz, CH_3CH_2OP); ^{31}P-NMR (81 MHz, $CDCl_3$): δ 31.20; IR (film): ν/cm^{-1} 2957, 2931, 1871, 1465, 1391, 1242, 1054, 1031, 963, 820, 788; MS-LR-CI (isobutane): m/z (%) 363 ($M^+ + 1$, 100); 235 ($M^+ + 1 - I$, 45); 154 (23); MS-LR-EI (70 eV): m/z (%) 235 ($M^+ - I$, 100); 207 (11); 179 (27); 152 (11); 149 (35); 137 (15); 125 (10); 121 (16); 97 (16); 81 (11); 55 (25); 41 (17); MS-HR-CI: $M^+ + 1$, found 363.0575, $C_{11}H_{25}O_3PI$ requires 363.0586.

Diethyl 3-iodo-n-octylphosphonate, ***3b***. Oil; preparative TLC on silica gel (petroleum ether–acetone = 2 : 1); yield 70% (purity 73% based on ^{31}P-NMR). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 0.88 (t, 3H, $^3J_{H-H} = 6.5$, C^8H_3); 1.32 (t, 6H, $^3J_{H-H} = 7.1$ Hz, 2 × CH_3CH_2OP); 1.24–2.09 [m, 12H, PCH_2CH_2, $C^4H_2(CH_2)_2C^7H_2$]; 4.09 (m, 5H, $2CH_3CH_2OP$, CH–I); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ 13.96 (s, C^8H_3); 16.39 (d, $^3J_{C-P} = 5.5$, CH_3CH_2OP); 22.43 (s, C^7H_2); 26.07 (d, $^1J_{C-P} = 141.26$, PC); 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, $^3J_{C-P} = 19.25$, CH–I); 40.33 (s, C^4H_2); 61.65 (d, $^2J_{C-P} = 6.4$ Hz, CH_3CH_2OP); ^{31}P-NMR ($CDCl_3$): δ 31.26; IR (film): ν/cm^{-1} 2979, 2956, 2929, 2871, 2836, 1467, 1437, 1391, 1366, 1096, 1056, 1030, 964, 788, 530; MS-LR-EI (70 eV): m/z (%) 249 ($M^+ - I$, 100); 137 (11); MS-LR-CI (isobutane): m/z (%) 377 ($M^+ + 1$, 100); 249 (73); MS-HR-CI: $M^+ + 1$, found 377.072 27; $C_{12}H_{27}O_3PI$ requires 377.074 25.

Diethyl 3-iodo-n-heptadecylphosphonate, ***3c***.

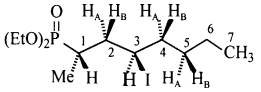


Non-distillable oil; m.p. 17.5–18.5 °C; column chromatography on silica gel (petroleum ether–acetone gradient); yield 52%. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.83 (t, 3H, $^3J_{H-H} = 7.0$, $C^{17}H_3$); 1.21 and 1.25–1.53 (br s and m, 24H, C^5H_2–$C^{16}H_2$); 1.28 (t, 6H, $^3J_{H-H} = 7.1$ Hz, 2 × CH_3CH_2OP); 1.61–1.68 (m,

1H, C^4H^A); 1.74–1.87 (m, 2H, PCH^A, C^4H^B); 1.92–2.04 (m, 3H, PCH^B, C^2H_2); 4.01–4.11 (m, 5H, 2 × CH_3CH_2OP, CH–I); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 13.90 (s, $C^{17}H_3$); 16.24 (d, $^3J_{C-P} = 5.9$, CH_3CH_2OP); 22.46 (s, $C^{16}H_2$); 25.85 (d, $^1J_{C-P} = 141.6$, PCH_2); 28.54, 29.13, 29.20, 29.32, 29.38, 29.42, 29.45, 31.70 (s, C^5H_2–$C^{15}H_2$); 33.26 (d, $^2J_{C-P} = 2.5$, C^2H_2); 39.00 (d, $^3J_{C-P} = 19.1$, C^3H–I); 40.18 (s, C^4H_2); 61.45 (2 × d, $^2J_{C-P} = 4.3$ Hz, CH_3CH_2OP); ^{31}P-NMR (81 MHz, $CDCl_3$): δ 31.22; IR (film): ν/cm^{-1} 2982, 2957, 2924, 2853, 1465, 1247, 1057, 1030, 962, 821, 792; MS-LR-CI (isobutane): *m/z* (%) 503 ($M^+ + 1$, 100); 375 ($M^+ - HI$, 38); MS-LR-EI (70 eV): *m/z* (%) 375 ($M^+ - I$, 100); MS-HR-CI: $M^+ + 1$, found 503.2126; $C_{21}H_{45}O_3PI$ requires 503.2151. Anal. found C 50.64, H 9.03, P 6.17; $C_{21}H_{44}O_3PI$ (502.45) requires C 50.20, H 8.82, P 6.16%.

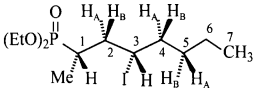
Reaction of 1b with 2a. The crude reaction mixture, obtained by the general procedure, was distilled using a Kugelrohr apparatus: 122 °C/0.01 mmHg, $n_D^{20} = 1.4680$, and then chromatographed using silical gel TLC plates and petroleum ether–acetone (2 : 1) as the eluent in order to separate the diastereoisomers **3d** ($R_F = 0.454$) and **3e** ($R_F = 0.380$). Overall yield 95% (purity 100% based on ^{31}P-NMR, **3d** : **3e** = 1 : 1).

Diethyl 3-iodo-1-methylheptylphosphonate (*trans*), ***3d***.



^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.91 (t, 3H, $^3J_{H-H} = 7.2$, C^7H_3); 1.19 (dd, 3H, $^3J_{H-H} = 7.1$, $^3J_{H-P} = 18.7$, $PCHCH_3$); 1.32 (2 × t, 6H, $^3J_{H-H} = 7.0$, 2 × CH_3CH_2OP); 1.27–1.47 (m, 3H, C^6H_2, C^5H^A); 1.49–1.59 (m, 1H, C^4H^A); 1.64–1.75 (m, 1H, C^5H^B); 1.77–1.84 (m, 1H, C^4H^B); 1.87–1.97 (m, 1H, C^2H^B); 2.09–2.20 [m, 2H, P(O)CH, C^2H^A]; 4.04–4.25 (m, 4H, 2 × CH_3CH_2OP); 4.35–4.39 (m, 1H, CH–I); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 13.92 (s, C^7H_3); 14.61 (d, $^2J_{C-P} = 4.7$, $PCHCH_3$); 16.47 (d, $^3J_{C-P} = 5.0$, CH_3CH_2OP); 21.88 (s, C^6H_2); 31.00 (d, $^1J_{C-P} = 141.04$, PCH); 31.40 (s, C^5H_2); 37.73 (d, $^3J_{C-P} = 7.39$, C^3H–I); 40.15 (s, C^4H_2); 42.71 (s, C^2H_2); 61.62 and 61.97 (2 × d, $^2J_{C-P} = 6.9$ Hz, CH_3CH_2OP); ^{31}P-NMR (81 MHz, $CDCl_3$): δ 33.73; IR (film): ν/cm^{-1} 2960, 2931, 2874, 2254, 1747, 1464, 1382, 1093, 1055, 1027; MS-LR-CI (isobutane): *m/z* (%) 249 ($M^+ - I$, 100), 166 (11), 69 (20), 55 (13); MS-LR-EI (70 eV): *m/z* (%) 377 ($M^+ + 1$, 100), 251 (15), 249 ($M^+ - HI$, 21); MS-HR-CI: $M^+ + 1$, found 377.072 10; $C_{12}H_{27}O_3PI$ requires 377.074 25.

Diethyl 3-iodo-1-methylheptylphosphonate (*cis*) ***3e***.



^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.91 (t, 3H, $^3J_{H-H} = 7.3$, C^7H_3), 1.12 (dd, 3H, $^3J_{H-H} = 7.1$, $^3J_{H-P} = 18.7$, $PCHCH_3$); 1.33 (2 × t, 6H, $^3J_{H-H} = 7.1$ Hz, 2 × CH_3CH_2OP); 1.27–1.46 (m, 3H, CH_3CH_2OP, C^5H^A, C^6H_2); 1.49–1.59 (m, 2H, C^5H^B, C^2H^A); 1.73–1.80 (m, 1H, C^4H^A); 1.90–1.98 (m, 1H, C^4H^B); 2.14–2.26 [m, 2H, P(O)CH, C^2H^B]; 4.06–4.17 (m, 5H, 2 × CH_3CH_2OP, CH–I); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 11.76 (d, $^2J_{C-P} = 5.05$, $PCCH_3$); 13.88 (s, C^7H_3); 16.46 (d, $^3J_{C-P} = 4.9$, CH_3CH_2OP); 21.90 (s, C^6H_2); 31.42 (d, $^1J_{C-P} = 142.08$, PCH); 31.64 (s, C^5H_2); 37.58 (d, $^3J_{C-P} = 18.01$, C^3H–I); 40.17 (s, C^2H_2); 40.93 (s, C^4H_2); 61.70 (2 × d, $^2J_{C-P} = 7.8$ Hz, $POCH_2CH_3$); ^{31}P-NMR (81 MHz, $CDCl_3$): δ 34.32; IR (film): ν/cm^{-1} 2959, 2929, 2859, 1460, 1243, 1146, 1096, 1055, 1028; MS-LR-CI (isobutane): *m/z* (%) 377 ($M^+ + 1$, 100); 249 ($M^+ - HI$, 33); MS-LR-EI (70 eV): *m/z* (%) 249 ($M^+ - I$, 100), 111 (19), 69 (33), 55 (19); HR-MS-CI: $M^+ + 1$, found 377.072 05; $C_{12}H_{27}O_3PI$ requires 377.0731.

2-Iodo-2-methylpropionitrile, 8. AIBN (1.04 g, 6.3 mmol) and molecular iodine (3.22–4.80 g, 12.6–18.9 mmol, see Table 3) were dissolved in benzene (25 mL) and refluxed with stirring for 4–6 h under argon atmosphere. The resulting solution was cooled to room temperature and decolorized with solid $Na_2S_2O_3$ (shaking with sodium thiosulfate for 1 min). Then, benzene was evaporated and the crude product was distilled using a Kugelrohr apparatus (115 °C/water pump) to give 0.65 g (53%, $n_D^{25} = 1.4980$) of the dark brown product. It was again dissolved in benzene and decolorized as described above with solid $Na_2S_2O_3$. After evaporation of benzene, the yellow product should be stored in a refrigerator to prevent decomposition. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.24; IR (film): ν/cm^{-1} 3281, 2949, 2242, 2229, 1745, 1682, 1471, 1390, 1380, 1109, 1204, 1060, 991, 705, 592; MS-EI (70 eV): *m/z* 195 (M^+, 27); 127 (I, 42); MS-CI (isobutane): *m/z* 196 ($M^+ + 1$); MS-HR-EI: M^+, found 195.9631; C_4H_7NI requires 195.9623.

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