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Highly stereoselective synthesis of functionalized 1,3-dienes from a new allyl bromide

Asma Fray[1], Jihène Ben Kraïem[2] and Hassen Amri[1,*]

[1]Department of Chemistry, University of Tunis El Manar, Faculty of Science, Campus, 2092 Tunis, Tunisia
[2]Laboratoire Méthodes et Techniques d'Analyse (LMTA), Institut National de Recherche et d'Analyse Physico-chimique (INRAP) Biotechnôpole Sidi-Thabet, 2020 Tunis, Tunisia.

Abstract: New and highly functionalized 1,3-dienes **3** and **4** have been synthesized *via* two different pathways starting from allyl bromide **1**. Firstly, the reaction of allyl bromide **1** with triethylphosphite leads to an allylphosphonate **2**, which undergoes the Wittig-Horner reaction with a range of saturated and unsaturated aldehydes gives rise to the corresponding 1,3-dienes **3**. Secondly, a highly stereoselective reaction between allyl bromide **1** and nitroalkane salts, offers the possibility to obtaining functionalized (*E*)-1,3-dienes **4**.

Keywords: Allyl bromide, allylphosphonate, 1,3-diene, nitroalkane, Wittig-Horner reaction.

Introduction

Functionalized 1,3-dienes have been attracting considerable interest as valuable products or key intermediates that are widely used in organic synthesis[1-4] and their preparation is an important goal for organic chemists. The 1,3-diene moiety can be found in a variety of bioactive natural products[5-8] including terpenoids, fatty acid-derived lipids, pheromones and polyketides[9-12], but they are also often used as a starting material for the synthesis of microbial metabolites such as rebeccamycin[13] or alkaloid arcyriaflavin-A[14] and many other compounds with antifungal and antiviral properties[15-19]. In addition, 1,3-dienes have been heavily involved in Diels-Alder reactions[20-22] and several efforts were made during this decade to provide new synthetic routes to 1,3-dienes in complex structures[23-38].

Previously, we have reported a new synthetic route to the diethyl (*E*)-1-(bromomethyl)-2-cyanovinylphosphonate **1**[39] and its application in the synthesis of new vinylphosphonates[40,41]. Following our interest in the synthesis of polyfunctionalized 1,3-dienes[42-44], we have sought to investigate, in the present work, the transformation of allyl bromide **1** into 1,3-dienes and the conditions of their preparation. For this purpose, we explored two ways which allow to obtain two families of 1,3-dienes **3** and **4** (Scheme 1), namely the use of allyl bromide **1** in an olefination type Wittig-Horner reaction (Route a) as well as its displacement using nitroalkane salts (route b).

**corresponding author:Hassen Amri*
E-mail address: hassen.amri@fst.rnu.tn
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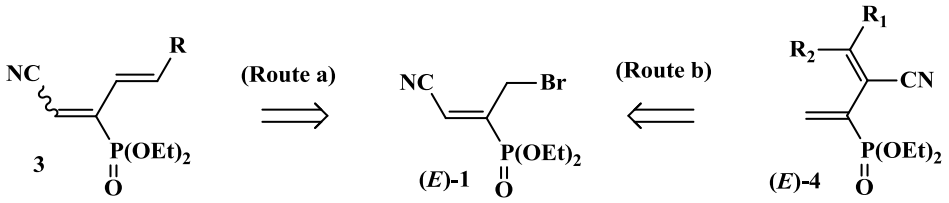
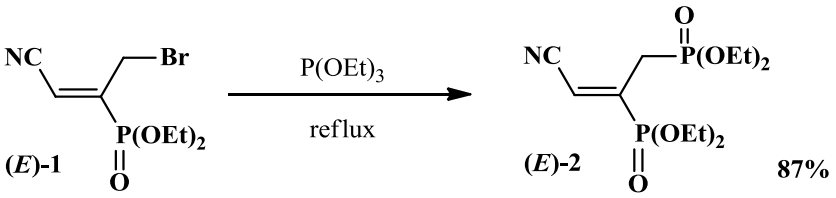


Scheme 1. Retrosynthetic routes to functionalized 1,3-dienes **3** and **4**.

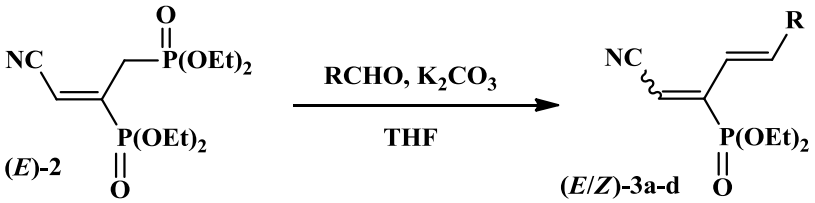
Results and Discussion

The conversion of the allyl bromide **1** to the corresponding allylphosphonate **2** has been carried out according to two procedures reported in the literature. Firstly, the use of the coupling reaction[45] of allyl bromide **1** with diethylphosphite in the presence of potassium carbonate as a base and tetrabutylammonium hydrogensulfate (TBAHS, 3 mol%) at 70°C, led to (*E*)-allylphosphonate **2** in low yield (23%). However, when a mixture of triethylphosphite-allyl bromide **1** was heated at 80°C without solvent, allylphosphonate **2** was isolated in 87% yield[46] (Scheme 2).



Scheme 2. (*E*)-Allylphosphonate **2** *via* the S_N2 substitution of (*E*)-allyl bromide **1**.

The next step is based on the Wittig-Horner type reaction of allylphosphonate **2** with a variety of aliphatic and aromatic aldehydes in the presence of anhydrous potassium carbonate in THF (Scheme 3), to isolate a new family of highly functionalized (*E,Z*)-1,3-dienes **3a-d** in good yields. The results depicted in Table 1 revealed that 1,3-dienes **3b-d** are obtained as a mixture of two stereoisomers (1*Z*,3*E*) and (1*E*,3*E*), whereas **3a** is isolated as a single stereoisomer (1*E*,3*E*). The stereochemistry of all dienes was ascertained by NOESY experiments.



Scheme 3. Wittig-Horner reaction of allylphosphonate **2** with various aldehydes.

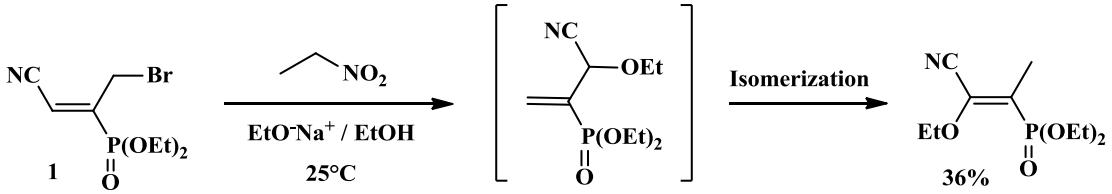
Table 1. Synthesis of functionalized 1,3-dienes **3a-d**

Diene	R	Time (h)	Rdt (%)[a]	(*E*/*Z*)[b]
3a	^{n}Bu	20	63	100/0
3b	4-Bromophenyl	24	75	68/32
3c	Furan-2-yl	24	78	60/40
3d	3-Bromo-4-methoxyphenyl	36	71	64/36

[a] *Yields refer to the pure isolated products characterized by ^{1}H, ^{31}P and ^{13}C NMR.*
[b] *Determined by ^{31}P NMR spectroscopy.*

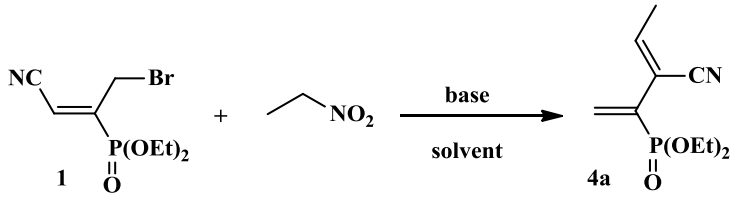
This motivating result prompted us to try another synthetic way to improve the yields of 1,3-dienes through the use of nitroalkane salts as nucleophilic reagents by assuming an easy S_N2' displacement of allyl bromide **1** and optimizing the formation of 1,3-dienes.

In our first study, we opted for the use of sodium ethoxide in ethanol to deprotonate nitroethane at room temperature which has unfortunately led to an ether instead of the expected 1,3-diene. This could be explained by the unexpected nucleophilic addition of ethanol, which reacts both as reagent and as solvent, to the double bond of bromide **1** to yield an allyl ether intermediate which rearranges into the corresponding vinyl isomer (Scheme 4).



Scheme 4. Undesirable side reaction of allyl bromide **1** with ethanol to provide vinyl ether.

In order to avoid this side reaction, we tried other bases and solvents (Table 2) and we found that the use of diluted sodium hydroxide in the presence of cetyltrimethylammonium bromide (CTABr) as catalyst gave 1,3-diene **4a** in modest yield (53%, entry 5), but the highest yield (94%) and the shortest reaction time (15 min) were achieved when the reaction of allyl bromide **1** with nitroethane (1.1 equiv.) was carried out in THF at room temperature in the presence of aqueous NaOH (0.6 M, 1.3 equiv.) without catalyst. The use of other bases such as DBU or DABCO was not conclusive (entries 2, 4). The overall results of this investigation are summarized in Table 2.

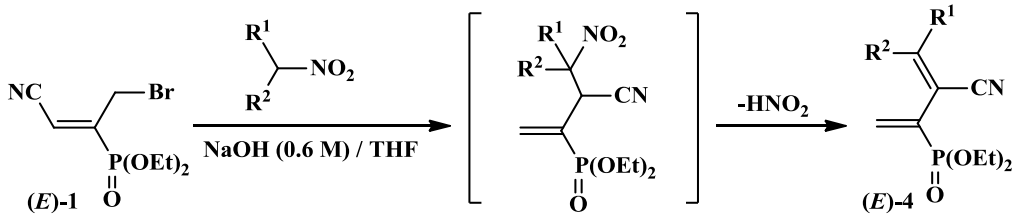


Scheme 5. Synthesis of 1,3-diene **4a** using various experimental conditions.

Table 2. Optimization of reaction conditions for the conversion of **1** into **4a**

Entry	Base	Base (equiv.)	Solvent	T °C	Time (h)	Rdt (%)
1	EtONa	1	EtOH	25	1	—
2	DBU	1	CH_3CN	25	1	32
3	NaOH (0.6 M)	1.3	THF/H_2O	0 to 25	0.25	94
4	DABCO	1.2	THF	50	2	10
5	NaOH	0.25/0.5	H_2O	25	1.5	53

Subsequently, we have extended this reaction to a wide variety of primary and secondary nitroalkanes to afford, under optimal reaction conditions, a new family of 2,3-difunctionalized 1,3-dienes **4a-d** in good to excellent yields (Table 3). As can be seen in Scheme 6, 1,3-dienes **4a-d** are obtained through S_N2'-type addition-elimination reaction of various nitronates with allyl bromide **1** followed by a loss of nitrous acid.



Scheme 6. Highly stereoselective synthesis of 2,3-difunctionalized 1,3-dienes **4a-d**

Table 3: Synthesis of (*E*)-2,3-difunctionalized-1,3-dienes **4a-d**.

1,3-Diene	R^1	R^2	Time (min)	Yield (%)*
4a	Me	H	15	94
4b	^{n}Pr	H	15	83
4c	^{n}Bu	H	15	79
4d	Me	Me	60	64**

**Yields refer to isolated products characterized by ^{1}H, ^{13}C NMR spectroscopy.*

***Functionalized 1,3-diene **4d** has been previously reported by Brel et al.*[47]

The stereochemistry of dienes **4a-d** has been assigned by the two-dimensional NMR (NOESY). The 1,3-diene **4a** shows no correlation between vinyl proton H (d, 6.28 ppm) and those of CH_3 (d, 2.16 ppm). This result indicates that H and CH_3 are not close to each other thus ascertaining the *E* configuration of the 1,3-diene **4a**.

Conclusion

In summary, we have successfully developed two simple and highly stereoselective methods for the synthesis of new polyfunctionalized 1,3-dienes **3** and **4** using firstly, the Wittig-Horner reaction of allylphosphonate **2** with some aliphatic and aromatic aldehydes and secondly, by means of the coupling reaction of allyl bromide **1** with nitroalkane salt.

Experimental Section

General. ^{1}H-NMR, ^{31}P-NMR and ^{13}C-NMR (fully decoupled) spectra were run on a Bruker AMX 300 spectrometer working at 300 MHz, 121 MHz and 75 MHz respectively for the proton, ^{31}P and ^{13}C in a pure deuterated $CDCl_3$ solvent and with tetramethylsilane (TMS) as the internal reference. The chemical shifts (δ) and coupling constants *(J)* are, respectively, expressed in parts per million (ppm) and Hertz (Hz). All NMR spectra were acquired at room temperature. Assignments of proton (^{1}H-NMR) and carbon (^{13}C-NMR) signals were secured by DEPT 135 and HMBC experiments. Multiplicity of peaks is indicated by the following: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; dq, doublet of quartets; m, multiplet. All reactions were monitored by TLC on silica gel plates (Fluka Kieselgel 60 F254, Merck) eluting with the solvents indicated, visualized by a 254 nm UV lamp and aqueous potassium permanganate solution. For column chromatography, Fluka Kieselgel 70-230 mesh was used. The main compounds were examined by Gas chromatography-mass spectrometry (GC/MS) and spectra were recorded on an Agilent Technologies 6890 N instrument with an Agilent 5973 N mass detector (EI) and an HP5-MS 30 m×0.25 mm capillary apolar column (stationary phase: 5% diphenyldimethylpolysiloxane film, 0.25 µm).

rt indicates the retention time. The elementary analyses (C, H, N) were performed on a Perkin–Elmer Series II CHNS / O Analyzer 2400.

Synthesis of (*E*)-Tetraethyl 3-cyanoprop-2-ene-1,2-diyldiphosphonate (2)

A solution of allyl bromide **1** (1 mol) and triethylphosphite (2 mol) was stirred at 80°C for one day. After completition, the reaction mixture was concentrated under reduced pressure to remove the rest of the triethylphosphite. The crude product was purified by flash chromatography (AcOEt) to obtain the diphosphonate **2**.

Brown liquid. Yield: 87 %. ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.32 (dd, 1H, $^{3}J_{HP}$ = 21 Hz, $^{4}J_{HP}$ = 6 Hz, =CH), 4.15 (dq, $^{3}J_{HP}$ = 7.5 Hz, J =7.5 Hz, 8H, $4OCH_2$), 3.16 (dd, 2H, $^{2}J_{HP}$ = 24 Hz, $^{3}J_{HP}$ = 18 Hz, CH_2), 1.36 (t, 12H, J = 7.5 Hz, $4CH_3$). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 146.3 (dd, =C, $^{1}J_{CP}$ = 178.5 Hz, $^{2}J_{CP}$ = 12 Hz), 114.0 (dd, =CH, $^{2}J_{CP}$ = 17.25 Hz, $^{3}J_{CP}$ = 12 Hz), 114.5 (d, CN, $^{3}J_{CP}$ = 6 Hz), 63.3 (d, $2OCH_2$, $^{2}J_{CP}$ = 5.25 Hz), 62.6 (d, $2OCH_2$, $^{2}J_{CP}$ = 6.75 Hz), 30.2 (dd, CH_2, $^{1}J_{CP}$ = 135.75 Hz, $^{2}J_{CP}$ = 8.25 Hz), 16.3 (d, $2CH_3$, $^{3}J_{CP}$ = 6 Hz), 16.2 (d, $2CH_3$, $^{3}J_{CP}$ = 6.75 Hz). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 20.58 (d, $^{3}J_{PP}$ = 8.47 Hz, P-CH_2), 12.40 (d, $^{3}J_{PP}$ = 8.47 Hz, =C-P). GC/MS (EI): rt = 33.73 min, *m/z* = 339 (M+, 22), 227 (62), 147 (100), 109 (25), 81 (36) 66 (46). Anal. calcd for $C_{12}H_{23}NO_6P_2$ (339,10): C, 42.48; H, 6.83; N, 4.13. Found: C, 41.69; H, 7.37; N, 3.87.

General procedure for the synthesis of 1,3-dienes 3a-d

A mixture of allyl bromide **1** (1 mmol), aldehyde (2 mmol) and potassium carbonate (2 mmol) in THF (3 mL) was stirred overnight at room temperature. Then, the mixture was hydrolyzed with water then extracted with ether (3×20 mL). The organic layers were washed with brine then dried over $MgSO_4$ and concentrated in vacuo. The obtained liquid was purified by column chromatography (Hexane-AcOEt, 6:4) to obtain 1,3-diene **3a-d**. The Z/*E*-diene isomers **3b-d** cannot be separated by column chromatography.

Diethyl (1E, 3E)-1-cyanohepta-1,3-dien-2-ylphosphonate (3a)

Yellow liquid. Yield: 63%.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.72 (m, 1H, =CH), 6.56 (m, 1H, =CH), 6.05 (d, 1H, $^{3}J_{HP}$ = 21 Hz, =CH), 4.12 (dq, $^{3}J_{HP}$ = 7 Hz, J = 7 Hz, 4H, $2OCH_2$), 2.23 (q, 2H, J = 7 Hz, CH_2), 1.51 (q, 2H, J = 8 Hz, CH_2), 1.36 (t, 6H, J = 7.5 Hz, $2CH_3$), 0.95 (t, 3H, J = 7.5 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 148.9 (d, =C, $^{1}J_{CP}$ = 169.5 Hz), 146.1 (d, =CH, $^{3}J_{CP}$ = 4.5 Hz), 124.1 (d, =CH, $^{2}J_{CP}$ = 7.5 Hz), 115.2 (d, CN, $^{3}J_{CP}$ = 28.5 Hz), 107.1 (d, =CH, $^{2}J_{CP}$ = 16.5 Hz), 62.9 (d, $2OCH_2$, $^{2}J_{CP}$ = 5.25 Hz), 35.8 (CH_2), 21.8 (CH_2), 16.2 (d, $2CH_3$, $^{3}J_{CP}$ = 6 Hz), 13.6 (CH_3). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 13.08. Anal. calcd for $C_{12}H_{20}NO_3P$ (257,12): C, 56.02; H, 7.84; N, 5.44. Found: C, 55.96; H, 7.89; N, 5.47.

Diethyl 4-(4-bromophenyl)-1-cyanobuta-1,3-dien-2-ylphosphonate (3b)

Yellow liquid. Yield: 75%.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.47–7.33 (m, 4H, H Ar), 7.24 (dd, 1H, $^{3}J_{HP}$ = 12 Hz, J = 6 Hz, =CH), 7.14 (d, 1H, J = 9 Hz, =CH), 6.1 (d, 1H, $^{3}J_{HP}$ = 18 Hz, =CH-*Z*), 6.05 (d, 1H, $^{3}J_{HP}$ = 21 Hz, =CH-*E*), 4.12 (dq, $^{3}J_{HP}$ = 7 Hz, J = 7 Hz, 4H, $2OCH_2$), 1.28 (t, 6H, J = 7.5 Hz, $2CH_3$). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 150.4 (d, =C-*Z*, $^{1}J_{CP}$ = 177 Hz), 148.3 (d, =C-*E*, $^{1}J_{CP}$ = 170.25 Hz), 139.9 (d, =CH, $^{3}J_{CP}$ = 3.75 Hz), 132.1 (s, CH Ar), 131.8 (s, C Ar), 130.0 (s, C Ar), 122.2 (d, =CH-*E*, $^{2}J_{CP}$ = 8.25 Hz), 121.6 (d, =CH-*Z*, $^{2}J_{CP}$ = 7.5 Hz), 129.1 (s, CH Ar), 115.2 (d, CN-*E*, $^{3}J_{CP}$ = 28.5 Hz), 114.5 (d, CN-*Z*, $^{3}J_{CP}$ = 31.5 Hz), 111.1 (d, =CH-*Z*,

$^{2}J_{CP}$ = 15.75 Hz), 108.7 (d, =CH-*E*, $^{2}J_{CP}$ = 15.75 Hz), 63.4 (d, 2OCH_2-*Z*, $^{2}J_{CP}$ = 6 Hz), 16.3 (d, 2CH_3, $^{3}J_{CP}$ = 6 Hz). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 12.49 (*E*); 11.51 (*Z*). Anal. calcd for $C_{15}H_{17}BrNO_3P$ (369,01): C, 48.67; H, 4.63; N, 3.78. Found: C, 48.72; H, 4.66; N, 3.81.

Diethyl 1-cyano-4-(furan-2-yl)buta-1,3-dien-2-ylphosphonate (3c)

Brown liquid. Yield: 78%.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.43 (d, 1H, *J* = 3 Hz, =CH), 6.39 (d, 1H, *J* = 3 Hz, =CH), 6.34 (d, 1H, *J* = 3 Hz, =CH), 6.24 (d, 1H, *J* = 9 Hz, =CH), 6.17 (d, 1H, $^{3}J_{HP}$ = 18 Hz, =CH-*Z*), 6.02 (d, 1H, $^{3}J_{HP}$ = 19.5 Hz, =CH-*E*), 5.81 (dd, 1H, $^{3}J_{HP}$ = 12 Hz, *J* = 6 Hz, =CH), 4.09 (dq, $^{3}J_{HP}$ = 7 Hz, *J* = 7 Hz, 4H, 2OCH_2), 1.28 (t, 6H, *J* = 7.5 Hz, 2CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 151.5 (=C), 150.3 (d, =C-*Z*, $^{1}J_{CP}$ = 177 Hz), 148.0 (d, =C-*E*, $^{1}J_{CP}$ = 169.5 Hz), 144.7 (=CH), 127.5 (d, =CH, $^{3}J_{CP}$ = 3.75 Hz), 123.4 (d, =CH-*E*, $^{2}J_{CP}$ = 11.25 Hz), 119.6 (d, =CH-*Z*, $^{2}J_{CP}$ = 7.5 Hz), 115.3 (d, CN-*E*, $^{3}J_{CP}$ = 28.5 Hz), 114.4 (s, =CH), 114.0 (d, CN-*Z*, $^{3}J_{CP}$ = 30.75 Hz), 112.5 (s, =CH), 111.7 (d, =CH-*Z*, $^{2}J_{CP}$ = 16.5 Hz), 107.3 (d, =CH-*E*, $^{2}J_{CP}$ = 16.5 Hz), 63.1 (d, 2OCH_2, $^{2}J_{CP}$ = 5.25 Hz), 16.2 (d, 2CH_3, $^{3}J_{CP}$ = 6.5 Hz). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 12.82 (*E*), 11.95 (*Z*). Anal. calcd for $C_{13}H_{16}NO_4P$ (281,08): C, 55.52; H, 5.73; N 4.98. Found: C, 55.56; H, 5.77; N 4.94.

Diethyl 4-(3-bromo-4-methoxyphenyl)-1-cyanobuta-1,3-dien-2-ylphosphonate (3d)

Greenish yellow liquid. Yield: 71%.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.67 (d, *J* = 9 Hz, 1H, H Ar), 7.47 (d, *J* = 9 Hz, 1H, H Ar), 7.23 (s, 1H, H Ar), 6.81 (dd, 1H, $^{3}J_{HP}$ = 15 Hz, *J* = 9 Hz, =CH), 6.69 (d, 1H, *J* = 9 Hz, =CH), 6.12 (d, 1H, $^{3}J_{HP}$ = 18 Hz, =CH-*Z*), 6.05 (d, 1H, $^{3}J_{HP}$ = 21 Hz, =CH-*E*), 4.12 (dq, $^{3}J_{HP}$ = 7 Hz, *J* = 7 Hz, 4H, 2OCH_2), 3.82 (s, 3H, CH_3), 1.32 (t, 6H, *J* = 7.5 Hz, 2CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 155.8 (s, C Ar), 150.7 (d, =C-*Z*, $^{1}J_{CP}$ = 176.25 Hz), 148.1 (d, =C-*E*, $^{1}J_{CP}$ = 168.5 Hz), 139.4 (d, =CH, $^{3}J_{CP}$ = 3.75 Hz), 133.1 (s, C Ar), 132.6 (s, C Ar), 129.1, 128.1 (s, CH Ar), 120.7 (d, =CH-*E*, $^{2}J_{CP}$ = 7.5 Hz), 120.4 (d, =CH-*Z*, $^{2}J_{CP}$ = 5.25 Hz), 115.1 (d, CN-*E*, $^{3}J_{CP}$ = 28.5 Hz), 114.6 (d, CN-*Z*, $^{3}J_{CP}$ = 30.75 Hz), 112.3 (s, CH Ar), 111.1 (d, =CH-*E*, $^{2}J_{CP}$ = 16.5 Hz), 107.6 (d, =CH-*Z*, $^{2}J_{CP}$ = 15.75 Hz), 63.4 (d, 2OCH_2, $^{2}J_{CP}$ = 6 Hz), 56.2 (OCH_3), 16.3 (d, 2CH_3, $^{3}J_{CP}$ = 6 Hz). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 12.84 (*E*), 11.78 (*Z*). Anal. calcd for $C_{16}H_{19}BrNO_4P$ (399,02): C, 48.02; H, 4.79; N, 3.50. Found: C, 47.86; H, 4.67; N, 3.41.

General procedure for the synthesis of 1,3-dienes 4a-d

A solution of allyl bromide ***E*-1** (1.0 mmol) in THF (3 mL) was added dropwise at 0 °C to a mixture of nitroalkane (1.1 mmol) and aqueous NaOH (1.3 mmol, 0.6 M). The resulting stirred mixture was warmed to room temperature until disappearance of the starting allyl bromide **1**. The reaction mixture was diluted with water and extracted with ether (3×20 mL). The organic phase was washed with brine (3 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography on a silica gel column, using (CH_2Cl_2 / AcOEt, 7:3) as eluent, gave pure functionalized 1,3-dienes **4a-d**.

(E)-Diethyl 3-cyanopenta-1,3-dien-2-ylphosphonate (4a)

Yellow liquid. Yield: 94 %.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.10 (q, 1H, *J* = 7 Hz, =CH), 6.38 (d, 1H, $^{3}J_{HP}$ = 12 Hz, =CH), 6.28 (d, 1H, $^{3}J_{HP}$ = 9 Hz, =CH), 4.12 (dq, $^{3}J_{HP}$ = 7 Hz, *J* = 7 Hz, 4H, 2OCH_2), 2.16 (d, 3H, *J* = 6 Hz, CH_3), 1.34 (t, 6H, *J* = 7.5 Hz, 2CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$)

δ = 147 (d, =CH, $^{3}J_{CP}$ = 2.25 Hz), 133.2 (d, =C, $^{1}J_{CP}$ = 180 Hz), 132.7 (d, =CH_2, $^{2}J_{CP}$ = 6 Hz), 114.8 (d, CN, $^{3}J_{CP}$ = 17.25 Hz), 114.1 (d, =C, $^{2}J_{CP}$ = 20.25 Hz), 62.7 (d, 2OCH_2, $^{2}J_{CP}$ = 6 Hz), 18.2 (CH_3), 16.2 (d, 2CH_3, $^{3}J_{CP}$ = 6 Hz). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 14.19. GC/MS (EI): rt = 46.56 min, *m/z* = 321 (67), 265 (51), 229 (M^+, 100), 109 (27), 81 (43), 65 (32). Anal. calcd for $C_{10}H_{16}NO_3P$ (229,09): C, 52.40; H, 7.04; N, 6.11. Found: C, 52.22; H, 6.97; N, 6.02.

(E)-Diethyl 3-cyanohepta-1,3-dien-2-ylphosphonate (4b)

Yellow liquid. Yield: 83 %.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.04 (t, 1H, *J* = 7.5 Hz, =CH), 6.41 (d, 1H, $^{3}J_{HP}$ = 9 Hz, =CH), 6.3 (d, 1H, $^{3}J_{HP}$ = 15 Hz, =CH), 4.12 (dq, $^{3}J_{HP}$ = 6.5 Hz, *J* = 6.5 Hz, 4H, 2OCH_2), 2.5 (q, 2H, *J* = 7 Hz, CH_2), 1.57 (sixtuplet, 2H, *J* = 7 Hz, CH_2), 1.34 (t, 6H, *J* = 6 Hz, 2CH_3), 0.98 (t, 3H, *J* = 7.5 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 152.0 (d, =CH, $^{3}J_{CP}$ = 2.25 Hz), 133.2 (d, =C, $^{1}J_{CP}$ = 180 Hz), 133.0 (d, =CH_2, $^{2}J_{CP}$ = 6 Hz), 114.9 (d, CN, $^{3}J_{CP}$ = 17.25 Hz), 113 (d, =C, $^{2}J_{CP}$ = 19.5 Hz), 62.7 (d, 2OCH_2, $^{2}J_{CP}$ = 6 Hz), 34.4 (CH_2), 21.8 (CH_2), 16.2 (d, 2CH_3, $^{3}J_{CP}$ = 6 Hz); 10.9 (CH_3). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 14.19. GC/MS (EI): rt = 48.93 min, *m/z* = 377 (65), 321 (25), 277 (30), 257 (M^+, 100), 109 (27), 81 (33) 65 (21). Anal. calcd for $C_{12}H_{20}NO_3P$ (257,12): C, 56.02; H, 7.84; N, 5.44. Found: C, 56.97; H, 7.72; N, 4.39.

(E)-Diethyl 3-cyanoocta-1,3-dien-2-ylphosphonate (4c)

Yellow liquid. Yield: 79 %.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.04 (t, 1H, *J* = 7.5 Hz, =CH), 6.4 (d, 1H, $^{3}J_{HP}$ = 9 Hz, =CH), 6.3 (d, 1H, $^{3}J_{HP}$ = 15 Hz, =CH), 4.12 (dq, $^{3}J_{HP}$ = 6.5 Hz, *J* = 6.5 Hz, 4H, 2OCH_2), 2.52 (q, 2H, *J* = 7 Hz, CH_2), 1.52 (sixtuplet, 2H, *J* = 6 Hz, CH_2), 1.45-1.36 (m, 2H, CH_2), 1.34 (t, 6H, *J* = 6 Hz, 2CH_3), 0.94 (t, 3H, *J* = 7.5 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 152.3 (d, =CH, $^{3}J_{CP}$ = 2.25 Hz), 133.2 (d, =C, $^{1}J_{CP}$ = 179.25 Hz), 132.9 (d, =CH_2, $^{2}J_{CP}$ = 6 Hz), 114.9 (d, CN, $^{3}J_{CP}$ = 17.25 Hz), 112.8 (d, =C, $^{2}J_{CP}$ = 20.25 Hz), 62.6 (d, 2OCH_2, $^{2}J_{CP}$ = 6 Hz), 32.3 (CH_2), 30.5 (CH_2), 22.2 (CH_2), 16.2 (d, 2CH_3, $^{3}J_{CP}$ = 6 Hz), 13.7 (CH_3). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 14.25. GC/MS (EI): rt = 50.79 min, *m/z* = 405 (83), 349(33), 291 (37), 271 (M^+, 100), 109 (28), 81 (33), 65 (21). Anal. calcd for $C_{13}H_{22}NO_3P$ (271,13): C, 57.55; H, 8.17; N, 5.16. Found: C, 57.79; H, 8.15; N, 4.93.

Diethyl 3-cyano-4-methylpenta-1,3-dien-2-ylphosphonate (4d)

Yellow liquid. Yield: 64 %.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.47 (d, 1H, $^{3}J_{HP}$ = 21 Hz, =CH), 5.96 (d, 1H, $^{3}J_{HP}$ = 45 Hz, =CH), 4.15 (dq, $^{3}J_{HP}$ = 6 Hz, *J* = 6 Hz, 4H, 2OCH_2), 2.17 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 1.36 (t, 6H, *J* = 6 Hz, 2CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 158.2 (d, =CH, $^{3}J_{CP}$ = 7.5 Hz), 136.9 (d, =CH_2, $^{2}J_{CP}$ = 9.75 Hz), 134.1 (d, =C, $^{1}J_{CP}$ = 183 Hz), 117.0 (d, CN, $^{3}J_{CP}$ = 17.25 Hz), 106.2 (d, =C, $^{2}J_{CP}$ = 19.75 Hz), 62.6 (d, 2OCH_2, $^{2}J_{CP}$ = 6 Hz), 24.4 (CH_3), 21.5 (CH_3), 16.2 (d, 2CH_3, $^{3}J_{CP}$ = 6 Hz). ^{31}P-NMR (121 MHz, $CDCl_3$) δ = 13.9. GC/MS (EI): rt = 25.59 min, *m/z* = 243 (M^+, 17), 187 (100), 169 (20), 122 (31)106 (22), 77 (25), 65 (16). Anal. calcd for $C_{11}H_{18}NO_3P$ (243,10): C, 54.32; H, 7.46; N, 5.76. Found: C, 54.46; H, 7.52; N, 5.74.

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References

1- (a) B. Tarnchompoo, C. Thebtaranonth, Y. Thebtaranonth, *Tetrahedron Lett*. **1987**, *28*, 6671–6674; (b) B. Tarnchompoo, C. Thebtaranonth, Y. Thebtaranonth, *Tetrahedron Lett.* **1987**, *28*, 6675-6678.
2- M. Kotera, J. M. Lehn, J. P. Vigneron, *Tetrahedron* **1995**, *51*, 1953-1972.
3- W. J. Bailey, R. L. Hudson, E. T. Yates, *J. Org. Chem*. **1963**, *28*, 828-831.
4- (a) Z. Rappoport, *The chemistry of dienes and polyenes*; Vol. 1. Chichester: *John Wiley & Sons* **1997**; (b) Z. Rappoport, *The chemistry of dienes and polyenes*; Vol. 2. Chichester: *John Wiley & Sons* **2001**.
5- X. Zhang, R. C. Larock, *Org. Lett*. **2003**, *5*, 2993-2996.
6- C. C. Yu, D. K. P. Ng, B. L. Chen, T. Y. Luh, *Organometallics* **1994**, *13*, 1487-1497.
7- B. E. Sime, B. Rickborn, J. M. Flournoy, I. B. Berlman, *J. Org. Chem*. **1988**, *53*, 4613-4616.
8- (a) E. I. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang, H. Hattori, *Acc. Chem. Res*. **2008**, *41*, 1474-1485; (b) J. S. Glasby, *Encyclopaedia of the Terpenoids*, Wiley, Chichester, UK, **1982**; (c) T. K. Devon, A. I. Scott, *Handbook of Naturally Occurring Compounds*, Vol. 2, Academic, New York, **1972**; (d) M. DellaGreca, C. D. Marino, A. Zarrelli, B. D'Abrosca, *J. Nat. Prod*. **2004**, *67*, 1492–1495; (e) F. Lv, Z. Deng, J. Li, H. Fu, R. W. M. van Soest, P. Proksc, W. Lin, *J. Nat. Prod*. **2004**, *67*, 2033-2036; (f) Y. Cheng, B. Schneider, U. Riese, B. Schubert, Z. Li, M. Hamburger, *J. Nat. Prod*. **2004**, *67*, 1854–1858; (g) E. W. Rogers, T. F. Molinski, *J. Nat. Prod*. **2005**, *68*, 450-452; (h) H. Mohamad, N. H. Lajis, F. Abas, A. M. Ali, M. A. Sukari, H. Kikuzaki, N. Nakatani, *J. Nat. Prod*. **2005**, *68*, 285-288.
9- A. –R. Han, M. –S. Kim, Y. H. Jeong, S. K. Lee, E. K. Seo, *Chem. Pharm. Bull*. **2005**, *53*, 1466-1468.
10- A. R. Pereira, J. A. Cabezas, *J. Org. Chem*. **2005**, *70*, 2594-2597.
11- J. A. Moreira, J. S. McElfresh, J. G. Millar, *J. Chem. Ecol*. **2006**, *32*, 169-194.
12- R. M. de Figueiredo, R. Berner, J. Julis, T. Liu, D. Turp, M. Christmann, *J. Org. Chem.* **2007**, *72*, 640-642.
13- M. Adeva, H. Sahagun, E. Caballero, R. Pelaez-Lamamie de Clairac, M. Medarde, F. Tome, *J. Org. Chem*. **2000**, *65*, 3387-3394.
14- M. Adeva, F. Buono, E. Caballero, M. Medarde, F. Tome, *Synlett* **2000**, 832-834.
15- D. Amans, V. Bellosta, J. Cossy, *Chem. Eur. J*. **2009**, *15*, 3457-3473.
16- G. Ramamoorthy, C. M. Acevedo, E. Alvira, M. A. Lipton, *Tetrahedron: Asymmetry* **2008**, *19*, 2546-2554.
17- M. Boldi, *Curr. Opin. Chem. Biol*. **2004**, *8*, 281-286.
18- Y. Liao, Y. –H. Hu, J. Wu, Q. Zhu, M. Donovan, R. Fathi, Z. Yang, *Curr Med. Chem*. **2003**, *10*, 2285-2316.
19- M. Kalesse, M. Christmann, *Synthesis* **2002**, 981-1003.

20- (a) O. Diels, K. Alder, *Liebigs Ann. Chem.* **1928**, *460*, 98–122; (b) F. Fringuelli, A. Taticchi, *The Diels-Alder Reaction: Selected Practical Methods*, West Sussex, England: *John Wiley & Sons* **2002**, 340; (c) J. Sauer, R. Sustmann, *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779-807; (d) S. Reymond, J. Cossy, *Chem. Rev.* **2008**, *108*, 5359-5406.
21- K. C. Nicolaou, S. A. Snyder, T. Montagnon, G. Vassilikogiannakis, *Angew. Chem., Int. Ed.*, **2002**, *41*, 1668-1698.
22- T. J. Brocksom, A. G. Correa, R. M. Naves, F. Silva, V. Catani, M. A. Ceschi, J. Zukerman-Schpector, A. P. Toloi, M. L. Ferreira, U. Brocksom, *Org. Synth. Theory Appl.* **2001**, *5*, 39-87.
23- S. Fustero, P. Bello, B. Fernandez, C. Del Pozo, G. B. Hammond, *J. Org. Chem*. **2009**, *74*, 7690-7696.
24- J. McNulty, P. Das, *Tetrahedron Lett*. **2009**, *50*, 5737-5740.
25- S. Laclef, C. J. Exner, M. Turks, V. Videtta, P. Vogel, *J. Org. Chem*. **2009**, *74*, 8882-8885.
26- L. J. Perez, H. L. Shimp, G. C. Micalizio, *J. Org. Chem*. **2009**, *74*, 7211-7219.
27- X. Huang, T. de Haro, C. Nevado, *Chem. Eur. J*. **2009**, *15*, 5904-5908.
28- H. –J. Zhang, Z. Song, C. Wang, C. Bruneau, Z. Xi, *Tetrahedron Lett*. **2008**, *49*, 624-627.
29- M. Ogasawara, H. Murakami, T. Furukawa, T. Takahashi, N. Shibata, *Chem. Commun*. **2009**, 7366-7368.
30- U. Uršič, U. Grošelji, A. Meden, J. Svete, B. Stanovnik, *Tetrahedron Lett*. **2008**, *49*, 3775-3778.
31- D. P. J. Hamon, P. R. Spurr, *Synthesis* **1981**, 873-879.
32- R. M. Davidson, G. L. Kenyon, *J. Org. Chem*. **1977**, *42*, 1030-1035.
33- M. F. Semmelhack, P. Helquist, L. D. Jones, L. Keller, L. Mendelson, L. S. Ryono, J. G. Smith, R. D. Stauffer, *J. Am. Chem. Soc*. **1981**, *103*, 6460-6471.
34- R. L. Cobb, J. E. Mahan, *J. Org. Chem*. **1977**, *42*, 2829-2832.
35- D. Bellus, C. D. Weis, *Tetrahedron Lett*. **1973**, *14*, 999-1000.
36- D. Bellus, K. Von Bredow, H. Sauter, C. D. Weis, *Helv. Chim. Acta* **1973**, *56*, 3004-3038.
37- M. G. Pettett, A. B. Holmes, *J. Chem. Soc., Perkin Trans. 1* **1985**, 1161-1165.
38- H. Kiji, T. Okano, E. Fujii, J. Tsuji, *Synthesis* **1997**, 869-870.
39- A. Fray, J. Ben Kraïem, A. Souizi, H. Amri, *Arkivoc* **2012**, *viii*, 119-127.
40- A. Fray, J. Ben Kraïem, H. Amri, *Heteroatom Chem*. **2013**, *24*, 460–465.
41- A. Fray, J. Ben Kraïem, A. Arfaoui, H. Amri, *Sci.World J*. **2014**, *2014*, Article ID 260325.
42- (a) F. Béji, J. Lebreton, J. Villiéras, H. Amri, *Tetrahedron* **2001**, *57*, 9959-9962; (b) F. Béji, J. Lebreton, J. Villiéras, H. Amri, *Synth. Commun*. **2002**, *32*, 3273-3278.
43- H. Kraïem, H. Amri, *Phosphorus, Sulfur and Silicon* **2007**, *182*, 2555-2564.
44- M. Ameur, A. Arfaoui, J. Ben Kraïem, S. S. Al-Deyab, H. Amri, *Med. J. Chem*. **2012**, *2*, 347-354.
45- T. Janecki, R. Bodalsky, *Synthesis* **1990**, 799-801.
46- D. Basavaiah, S. Pandiaraju, *Tetrahedron* **1996**, *52*, 2261-2268.
47- V. K. Brel, E. V. Abramkin, *Zh. Obshch. Khim*. **1994**, *64*, 1989-1994.