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Acid-promoted transformations of 1-(diphenylphosphoryl)allenes: synthesis of novel 1,4-dihydrophosphinoline 1-oxides

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Keywords: allenes, 1-phenyl-1,4-dihydrophosphinoline 1-oxides, 3-hydroxyalk-2-en-1-yl-diphenylphosphine oxides, phosphaheterocycles, Bronsted and Lewis acids and superacids

Abstract: 1-(Diphenylphosphoryl)alka-1,2-dienes (phosphonoallenes) in Bronsted (super)acids (TfOH, FSO$_3$H, H$_2$SO$_4$) at -70 ÷ 120 °C for 30 min - 4 h give, at first, 3-hydroxyalk-2-en-1-yl-diphenylphosphine oxides, as kinetically favorable reaction products, that are further converted into 1-phenyl-1,4-dihydrophosphinoline 1-oxides, as thermodynamically stable compounds. The latter compounds are formed from phosphonoallenes under the action of strong Lewis acid AlCl$_3$ at room temperature for 10-120 min. This is novel, simple and efficient (short reaction time, high yields) method of synthesis of such 1,4-dihydrophosphinoline 1-oxides.

Graphical Abstract:
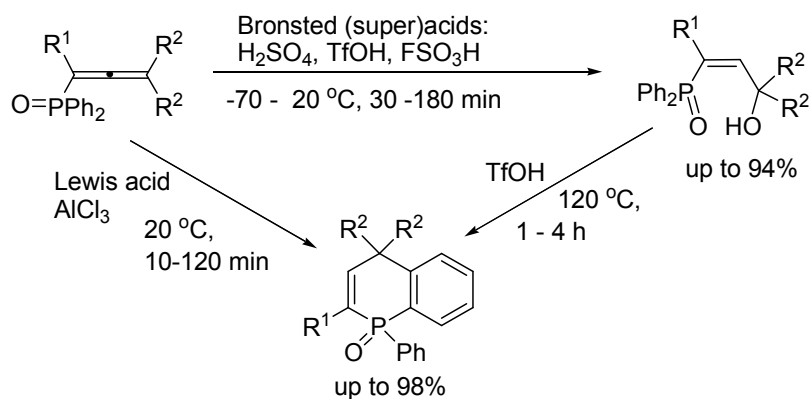
Allenes attracts increasing attention in organic synthesis, both as interesting building blocks and synthetic targets.[1] The synthetic potential of functionalized allenes has been explored extensively in recent years, and this has led to development of novel methods for construction of a variety of functionalized heterocyclic and carbocyclic systems.[2] One of characteristic reactions of allenes is electrophilic addition. The interactions of electrophiles, including the hydrohalogenic acids, with dialkyl allenephosphonates[3] or allenylphosphine oxides[4] lead to formation of 2,5-dihydro-1,2-oxaphosphole derivatives or expected 2,1- or 2,3-adducts, depending on substituents at the terminal carbon atoms of the allene system.

Based on our previous studies on substituted phosphonoallenes[5] in this work we have investigated reactions of 1-(diphenylphosphoryl)allenes **1** under the action of Bronsted acids (H_2SO_4), superacids (TfOH, FSO_3H), and strong Lewis acid (AlX_3, X = Cl, Br). While a number of studies on transformations of alkenes and alkynes under superelectrophilic activation conditions have already been reported,[6] but allenes remain vastly underexplored in these reactions.

The necessary initial allenes **1a-g** were obtained in reaction of the corresponding propargyl alcohols with chloro diphenyl phosphine in yields of 55-65% as it was described by us previously[5] (Figure 1).
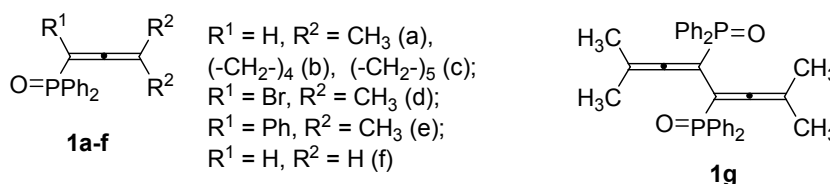

Figure 1. Initial 1-(diphenylphosphoryl)alka-1,2-dienes **1a-g**.

One may expect the following acid-promoted transformations of allene **1** (Scheme 1). Protonation of oxygen atom of the group P=O and allene triad results in the formation of cation **A**, which may react in two different ways: a) 6-*endo-trig* cyclization into phenyl ring, leading to 1-phenyl-1,4-dihydrophosphinoline-1-oxide **2**; b) interaction with oxygen atom of the group P=O, giving cation **B**, hydrolytic cleavage of the latter forms 3-hydroxyalk-2-en-1-yl-diphenylphosphine oxide **3**.

In case of Lewis acids, their coordination on oxygen atom and allene system takes place giving species **C** (Scheme 1). For powerful Lewis acids, such as $AlCl_3$ or $AlBr_3$, a strong coordination with oxygen atom of the group P=O may be occurred, leading to complete deactivation of nucleophilic properties of this oxygen. As a result, formation of alcohol **3** may be fully suppressed, and appearance of phospinoline oxide **2** is expected as the only reaction product.
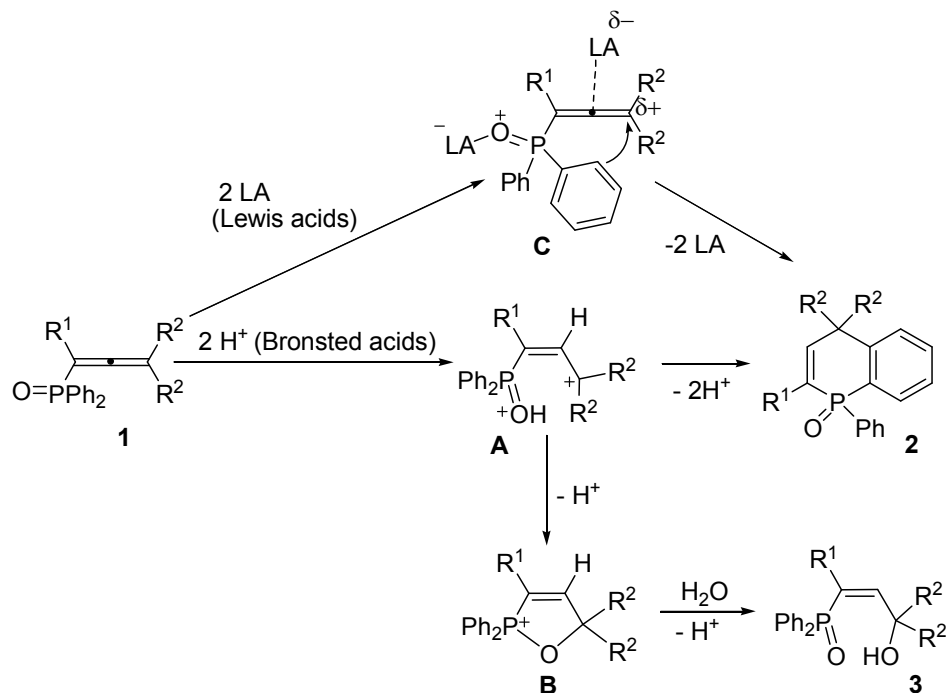
Scheme 1. Acid-promoted transformations of allenes **1**.

It is worth noting that such 1-phenyl-1,4-dihydrophosphinoline 1-oxides **2** have not been previously described yet. To the best of our knowledge, at the moment there are only a few methods for synthesis of these phosphaheterocycles. They are based on reactions of 1-chloro-1,2,3,4-tetrahydrophosphinoline 1-oxide[7] and benzophosphole ring expansion.[8] The compound **2** may be of great importance as phosphorus ligands and also as corresponding phosphine precursors in coordination chemistry of transition metals.

Indeed, acid-promoted transformations of allenes **1a-g** give two kinds of reaction products phosphinoline oxides **2a-f** and alcohols **3a-f** depending on the structure of initial allene, acid (Bronsted or Lewis), and reaction conditions (temperature, time). The obtained results are presented in Tables 1, 2. Structures of reaction products were determined by ^{1}H, ^{13}C, ^{31}P NMR, HRMS, IR spectrometry (see Supplementary material) and X-ray analysis (see Figure 2). Compounds **3a-f** are exclusively formed as Z-isomers, that was proved by values of coupling constants ^3J ~12 Hz for vicinal protons at bond C=C (see Supplementary material) and by X-ray data (see Figure 2).

Table 1. Acid promoted reactions of allene **1a**.
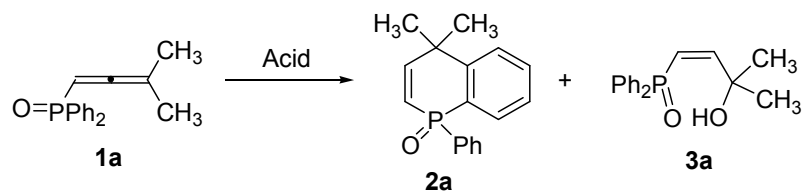
Entry	Acid	Reaction conditions		Reaction products; yield, %	
		Temperature,°C	Time, h	**2a**	**3a**
1	CF$_3$CO$_2$H (35 equiv)	20	0.5	-[a]	-
2	H$_2$SO$_4$ (50 equiv)	20	0.5	14	84
3	H$_2$SO$_4$ (50 equiv)	20	50	12	85
4	TfOH (38 equiv)	20	0.5	5	94
5	TfOH (38 equiv)	120	1	78	17
6	TfOH (38 equiv)	120	4	88	3
7	FSO$_3$H (50 equiv)	-40	3	18	80
8	FSO$_3$H (50 equiv)	-70	3	27	71
9	**AlCl$_3$ (5 equiv)–CH$_2$Cl$_2$**	**20**	**0.17**	**98**	**-**
10	AlBr$_3$ (5 equiv)–CH$_2$Cl$_2$	20	0.17	74	-
11	SnCl$_4$ (5 equiv)–CH$_2$Cl$_2$	20	0.17	-[a]	-
12	TiCl$_4$ (5 equiv)–CH$_2$Cl$_2$	20	0.17	-[a]	-
13	ZnCl$_2$ (5 equiv)–CH$_2$Cl$_2$	20	0.17	-[a]	-
14	FeCl$_3$ (5 equiv)–CH$_2$Cl$_2$	20	0.17	-[a]	-

[a]Quantitative recovery of unreacted initial **1a** after reaction.

First, we checked transformations of allene **1a** in various acidic systems (Table 1). In Bronsted acid H$_2$SO$_4$ (CF$_3$CO$_2$H is too weak) and superacids TfOH, FSO$_3$H both phosphinoline oxide **2a** and alcohol **3a** are formed in whole high yields (Entries 1-8). The series of experiments in TfOH has shown that yield of the compound **2a** is growing up with increasing of reaction time and temperature (from 20 to 120°C) (Entries 4-6). Also individually isolated alcohol **3a** in TfOH at 120°C for 4 h was completely converted into compound **2a**. These data reveal that formation of alcohol **3a** is kinetically favorable and reversible, and it goes to more thermodynamically stable phosphinoline oxide **2a**.

It is amazing, under the action of strong Lewis acid AlCl$_3$ at room temperature for just 10 min the only reaction product is the quantitatively formed compound **2a** (Entry 9). It should be mentioned that the necessary amount of AlCl$_3$ is at least 5 molar excess, smaller charges of AlCl$_3$ decrease dramatically the reaction product yield. AlBr$_3$ also promotes this transformation but gives less yield of phosphinoline oxide **2a** in 74%, the rest is unidentified compounds, and again no traces of alcohol **3a** are detected (Entry 10). Weaker Lewis acids are not reactive at all at the same reaction conditions (Entries 11-14). Effect of Lewis acids AlX$_3$ (X = Cl, Br) may be explained by strong coordination of this Lewis acid at oxygen atom of the group P=O in intermediate structure **C** (Scheme 1), that fully deactivates this oxygen for further electrophilic attack on it.
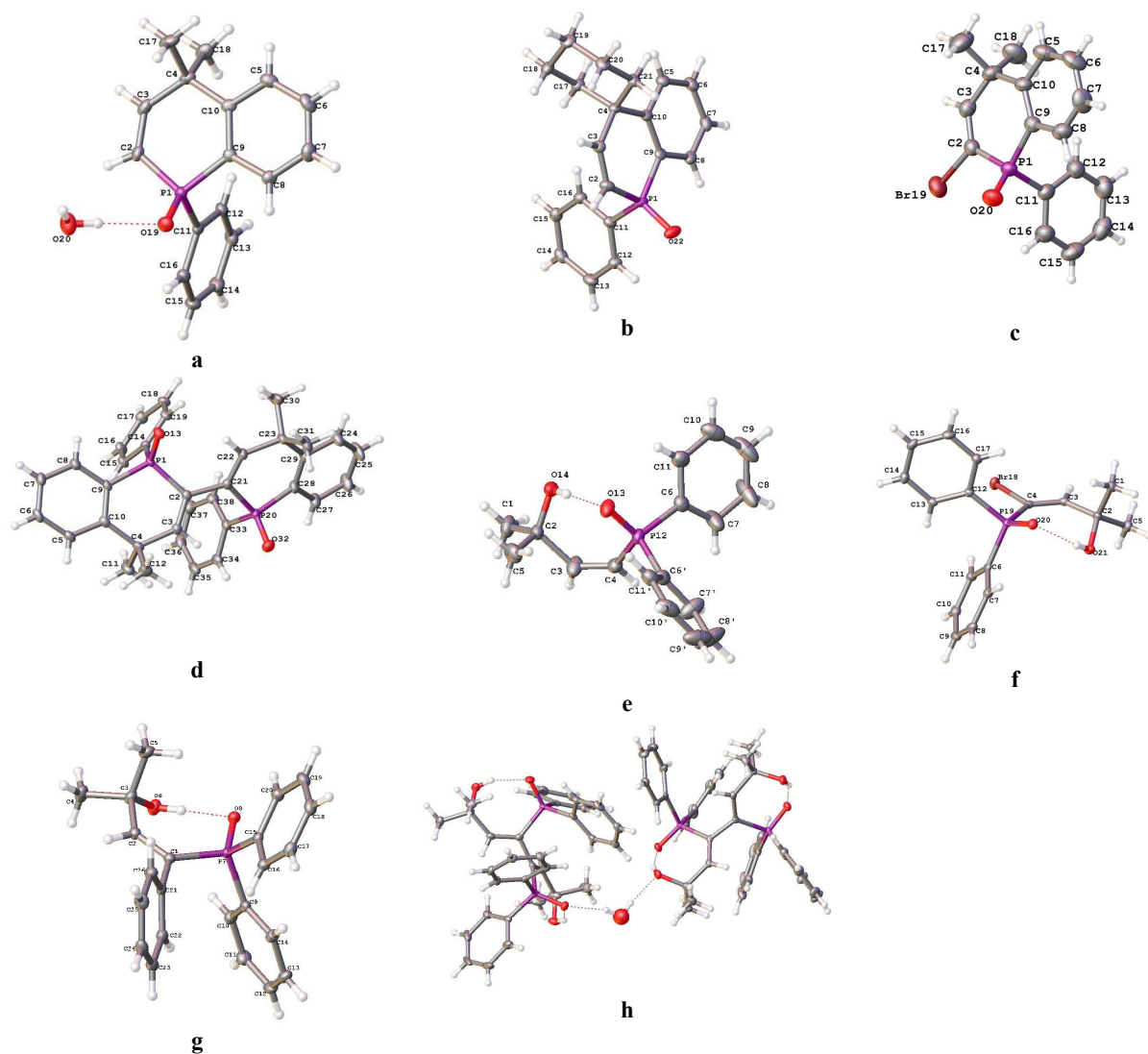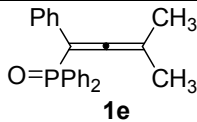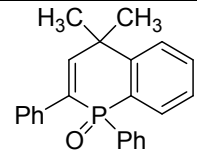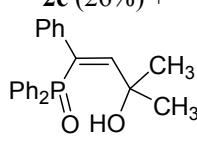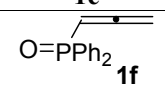
Figure 2. X-ray crystal structures of compounds **2a** (a), **2c** (b), **2d** (c), **2f** (d), **3a** (e), **3d** (f), **3e** (g), **3f** (h), structures **2a**, **3f** contain cocrystallised molecule of water (ORTEP diagrams, CCDC reference numbers: **2a** – CCDC 10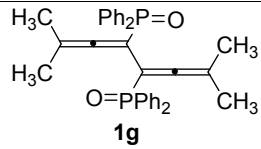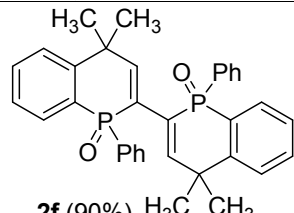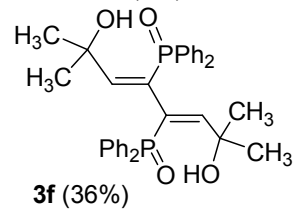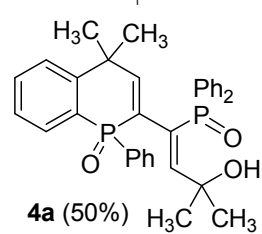26531, **2c** – CCDC 1026529, **2d** – CCDC 1026527, **2f** – CCDC 1026526, **3a** – CCDC 1029399, **3d** – CCDC 1026528, **3e** – CCDC 1029400, **3f** – CCDC 1026532).

Similar regularities are observed for transformations of other allenes **1b-g** (Table 2). Reactions with AlCl$_3$ result in the formation of corresponding phosphinoline oxide **2b-f** at room temperature for 10-120 min in high yields (Entries 1, 4, 9, 15, 24). Playing with various Bronsted (super)acids, reaction temperature and time allows to obtain exclusively alcohols **3b-f** (Entries 2, 3, 5-8) or to achieve predominant formation of compounds **2b-f** (Entries 10, 13, 26, 27).

Table 2. Acid promoted reactions of allenes **1b-g**.
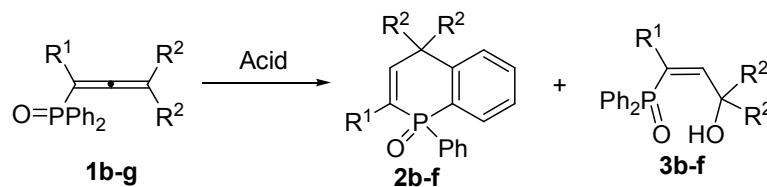
Entry	Allene	Acid	Reaction conditions		Reaction products, yield (%)
			Temperature, °C	Time, h	
1	**1b** (O=PPh₂ allene cyclopentane)	AlCl₃	20	0.17	**2b** (57%)
2	**1b**	H₂SO₄	20	0.5	**3b** (47%)
3	**1b**	FSO₃H	-70	1	**3b** (70%)
4	**1c** (O=PPh₂ allene cyclohexane)	AlCl₃	20	0.17	**2c** (50%)
5	**1c**	H₂SO₄	20	0.5	**3c** (52%)
6	**1c**	TfOH	20	0.75	**3c** (13%)
7	**1c**	TfOH	-40	3	**3c** (51%)
8	**1c**	FSO₃H	-40	3	**3c** (90%)
9	**1d** (Br, CH₃, O=PPh₂, CH₃)	AlCl₃	20	0.75	**2d** (80%)
10	**1d**	H₂SO₄	20	0.5	**2d** (14%) + **3d** (85%)
11	**1d**	TfOH	20	0.5	**2d** (17%) + **3d** (81%)
12	**1d**	TfOH	20	40	**2d** (31%) + **3d** (67%)
13	**1d**	TfOH	120	1	**2d** (91%) + **3d** (2%)
14	**1d**	FSO₃H	-40	3	**2d** (31%) + **3d** (67%)

15	**1e**	AlCl$_3$	20	2	**2e** (62%)
16	**1e**	H$_2$SO$_4$	20	0.5	**2e** (26%) + **3e** (72%)
17	**1e**	TfOH	20	0.5	**2e** (14%) + **3e** (80%)
18	**1e**	TfOH	120	1	**2e** (34%) + **3e** (2%)
19	**1e**	FSO$_3$H	-40	3	**2e** (18%) + **3e** (80%)
20	**1e**	FSO$_3$H	-70	1	**2e** (30%) + **3e** (68%)
21	**1f**	AlCl$_3$	20	0.17	oligomeric materials
22	**1f**	H$_2$SO$_4$	20	0.5	-[a]
23	**1f**	TfOH	120	1	oligomeric materials
24	**1g**	AlCl$_3$	20	2	**2f** (90%)
25	**1g**	H$_2$SO$_4$	20	0.5	-[a]
26	**1g**	TfOH	120	1	**2f** (4%) + **3f** (36%) + **4a** (50%)
27	**1g**	TfOH	120	3	**2f** (2%) + **3f** (38%) + **4a** (48%)

[a]Quantitative recovery of unreacted initial allene after reaction.

Having no substituents in allene triad, 1-(diphenylphosphoryl)allene **1f** gives with both $AlCl_3$ and TfOH complex mixtures of oligomeric materials (Entries 21, 23), due to instability and high reactivity of corresponding intermediate cations **A** and **C** (Scheme 1).

Depending on reaction conditions bis-allene **1g** may form three kinds of reaction products: bis-phosphinoline oxide **2f**, bis-alcohol **3f**, and mixed phosphinoline oxide – alcohole structure **4a** (Entries 24-27).

It is interesting to trace effect of substituent R^1 to ratio of reaction products **2** : **3**. Thus, allenes **1a,d,e** with R^2 = CH_3, differing in groups R^1 = H, Br, Ph, correspondingly, give mixtures of phosphinoline oxides **1a,d,e** and alcohols **3a,d,e** at the same reaction conditions in H_2SO_4 (see Table 1, Entry 2; Table 2, Entries 10, 16). For the compounds **1a** (R^1 = H) and **1d** (R^1 = Br) the ratio of **2** : **3** is 1 : 6 (Table 1, Entry 2; Table 2, Entry 10). But in case of R^1 = Ph for allene **1e**, amount of alcohol is reduced, and the ratio of **2e** : **3e** is 1 : 2.7 (Table 2, Entry 16). In terms of the intermediate cations **A** (Scheme 1), positive charge may be partially delocalized into substituent R^1 in these species. When R^1 = Ph this delocalization may play a big role, leading to a substantial decrease of charge on reactive carbocationic center, that hampers nucleophilic attack from oxygen in the way to cation **B** (Scheme 1). That finally results in the decrease of amount of the corresponding alcohol **3**.

It should be noted recently various phosphonoallenes have been widely explored in intra- and inter-molecular processes of carbo- and hetero-cycles formations: indenes, indenones, naphthalenes, phenanthrenes, furans, indols, (iso)chromenes, isocoumarins, thiochromanes.[9]

In conclusion, novel and efficient syntheses of 1-phenyl-1,4-dihydrophosphinoline 1-oxides and 3-hydroxyalk-2-en-1-yl-diphenyl phosphine oxides based on acid-promoted transformations of 1-(diphenylphosphoryl)alka-1,2-dienes have been developed. The scope, limitations, and mechanistic aspects of the reaction are under current investigation.

General procedure for transformation of compounds 1a-g in Bronsted acids (TfOH, FSO_3H, H_2SO_4). Synthesis of compounds 2a-g, 3a-g, 4a.

A solution of allene **1** (0.3 mmol) in TfOH (1 mL) was stirred at temperature for the time as indicated in Tables 1,2. The mixture was poured into ice water (30 mL) and extracted with chloroform (3×30 mL). The extracts were combined, washed with water, a saturated aqueous solution of $NaHCO_3$, and water again, and dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatographic separation on silica gel using CH_2Cl_2–MeOH (up to 5 %) as an eluent.

Analogously the reactions were carried out in HSO_3F and H_2SO_4 (see Tables 1, 2).

General procedure for transformation of compounds 1a-g under the action of AlCl₃. Synthesis of compounds 2a-g.

AlCl₃ (2.5 mmol) was added to solution of allene **1** (0.5 mmol) in CH_2Cl_2 (10 mL). Reaction mixture was stirred at 20°C for 10-120 min as indicated in Tables 1,2. The mixture was quenched with ice water (50 mL) and extracted, and worked-up as described above.

Supplementary material: general remarks, ^{1}H, ^{13}C, ^{31}P NMR spectra, X-ray data.

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