Utilization of the ArH–PCl_3–$AlCl_3$ Reaction Product as the Source of Phosphorus in the Phosphetane Synthesis of McBride, *et al.*

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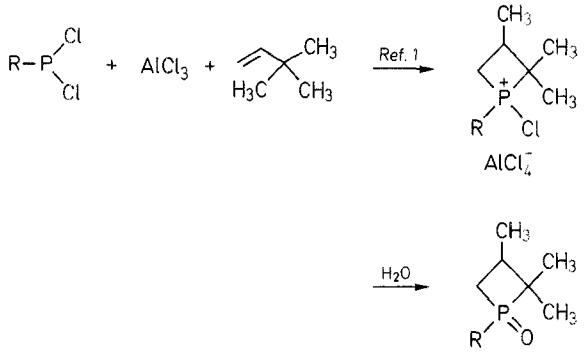
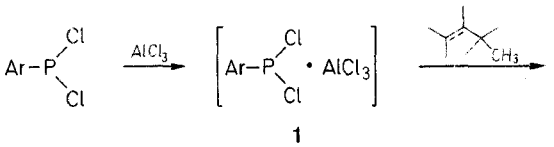
A variation of the phosphetane 1-oxide synthesis of McBride, *et al.*, is described, in which, instead of arylphosphonous dihalide, the *in situ* reaction of arenes with phosphorus trichloride-aluminum trichloride is used in a one-pot approach. Reaction of the complex formed with 3,3-dimethyl-1-butene or 2,4,4-trimethyl-2-pentene results in the formation of *cis/trans* mixtures of 1-aryl-2,2,3-trimethylphosphetane 1-oxides or 1-aryl-2,2,3,4,4-pentamethylphosphetane 1-oxides, respectively, in which the *trans* isomer predominates.

The major method for the construction of the phosphetane ring system remains that described nearly 25 years ago by McBride, et al.[1] This consists of the aluminum chloride-catalyzed reaction of phosphonous dihalides (or phosphorus trihalides) with certain branched-chain alkenes, as in the example below.



A drawback in the synthesis of *P*-arylphosphetane oxides is that arylphosphonous dihalides, with the exception of the phenyl compound, are not readily available and are all highly reactive, malodorous materials that are difficult to work with. This has limited the scope of the process, and very few substituted-phenyl phosphetane oxides have been prepared by this process. Such compounds are probably easier to obtain by the longer process of preparing the 1-chlorophosphetane oxide and then reaction with an arylmetallic reagent.[2] Following our discovery that oxygen-insertion by peroxyacids into the strained C-P bond of the phosphetane ring constitutes a simple method for making new types of 1,2-oxaphospholanes,[3] our interest became directed to the phosphetane oxide synthesis problem. We now report on a procedure that eliminates the direct use of arylphosphonous dihalides in the reaction with alkenes, at the same time making available a range of substituted-arylphosphetane oxides.

The $ArPX_2$–$AlCl_3$-alkene combination of the process of McBride, *et al.*,[1] may start with the well-known complexing of the first two reactants, followed by attack on the alkene. A carbocation rearrangement is necessary before the 4-membered ring can be closed.



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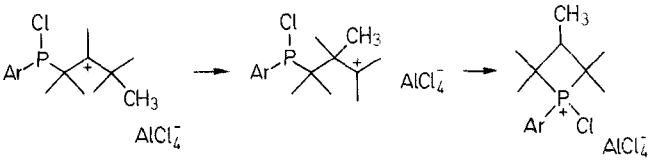
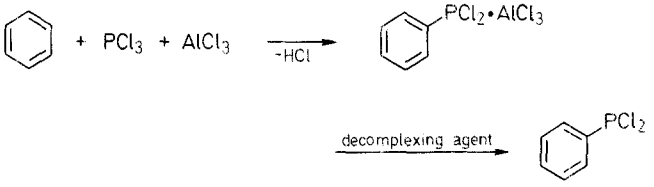
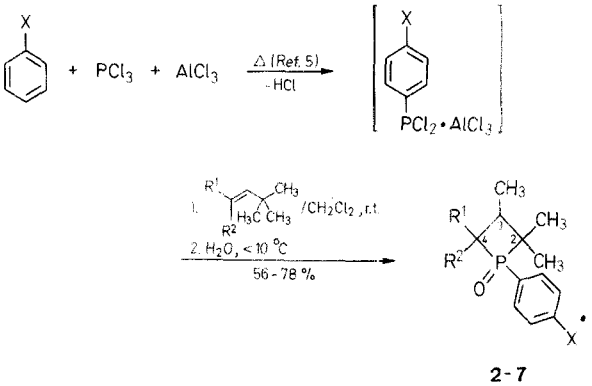


We have recognized that the complex **1** is of the same type as formed in the electrophilic substitution on the benzene ring by the combination of aluminum trichloride and phosphorus trichloride.



The break-up of this complex is difficult, and has posed a severe limitation in the use of this process, which nevertheless is considered as a standard method for arylphosphonous dichloride synthesis.[4] We were therefore led to use this complex *directly* in the reaction with branched alkenes, and indeed were successful in preparing phosphetanes in this fashion. The overall process is represented below.



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Product	R^1	R^2	X
2	H	H	H
3	CH_3	CH_3	H
4	H	H	Cl
5	CH_3	CH_3	Cl
6	H	H	F
7	CH_3	CH_3	F

The arene-PCl_3–$AlCl_3$ reaction is conducted at reflux using an excess of phosphorus trichloride, as is described in *Organic Syntheses*.[5] The excess phosphorus trichloride is then removed by vacuum distillation, and dichloromethane is added as solvent for the reaction with the alkene, which is conducted at room

temperature. Work-up follows the McBride, *et al.*, procedure.[1] This new process therefore completely eliminates the prior synthesis of the arylphosphonous dichlorides and any handling of such materials. The overall yields of phosphetane oxides **2**[6] and **3**[6] (Table 1) were quite satisfactory (80% and 72%, respectively, from benzene), and appear to exceed those of the original process, although the data may not be strictly comparable. The products of the process of McBride, *et al.*, are mixtures of *cis, trans* isomers. The workup procedure strongly influenced the ratio;[7] the conditions used in our work always gave the *trans* isomer in predominance.

The process was next applied to the synthesis of several halophenylphosphetane oxides, using chlorobenzene and fluorobenzene as starting materials. The yields of *trans, cis* mixtures **(4–7)** that resulted are given in Table 1. Samples could be enriched in the *trans* isomer (> 90%) by chromatography, and such samples were used for elemental analysis.

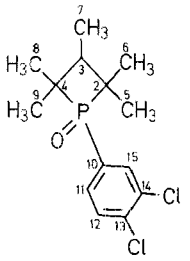
Table 1. Synthesis of 1-Arylphosphetane 1-Oxides[a]

Product	Yield[b] (%)	Molecular Formula[c]	^{31}P-NMR[d] δ (ppm) *trans*	*cis*
2	80	–	43.8	52.2
3	72	–	53.6	–
4	56	$C_{12}H_{16}ClOP$ (242.7)	43.6	48.6
5	77	$C_{14}H_{20}ClOP$ (270.7)	52.3	55.6
6	65	$C_{12}H_{16}FOP$ (226.2)	43.4	51.7
7	78	$C_{14}H_{20}FOP$ (254.3)	52.8	55.3
8	46	$C_{14}H_{19}Cl_2OP$ (305.2)	52.6	54.5

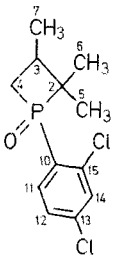
[a] *cis/trans* mixtures.
[b] Yields of recrystallized product.
[c] Satisfactory microanalyses obtained: C ±0.21, H ±0.17, P ±0.21.
[d] $CDCl_3$ solutions; values downfield from 85% H_3PO_4 as reference.

While it is possible that small amounts of *ortho* or *meta* isomers were formed in the substitutions on the benzene ring,[4] there was no spectral evidence that the final phosphetane oxides contained these position isomers. Thus, the ^{31}P-NMR spectra possessed signals only for the *trans* and *cis* isomers, with the *trans* always at higher field. The ^{13}C-NMR spectra (Table 2) for the isomer mixtures only showed the characteristic *para*-substitution pattern. Apparently any position isomers are lost during the isolation procedure. The complete interpretation of the ^{13}C-NMR spectra followed that of previous investigators.[6] The ^{13}C spectrum of *trans*-**6** has been previously reported,[6] but no details on its synthesis or other properties have appeared in the literature.

The isomeric dichlorobenzenes were also used in the process, but only with the *ortho* isomer were satisfactory results (46% yield) obtained. From this halide, the 3,4-dichlorophenyl product should greatly predominate over the 2,3-dichlorophenyl isomer; in the reaction with 2,4,4-trimethyl-2-pentene, the two signals on the ^{31}P-NMR spectrum were presumed to be to the *trans* (δ = 52.6 ppm) and *cis* (δ = 54.5 ppm) isomers of **8**, formed in an 8 to 1 ratio as determined by ^{31}P-NMR spectroscopy. The elemental analysis and ^{13}C-NMR spectrum (Table 2) were obtained on the mixture.



8 (46%)



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m-Dichlorobenzene gave a poor yield (20%) of a product in the reaction with 3,3-dimethyl-1-butene that was apparently a mixture of positional and geometric isomers. Enough of the major isomer (^{31}P-NMR signal at δ = 47.7 ppm) was isolated by chromatography so as to permit the collection of ^{13}C-NMR data (Table 2). The most probable structure is *trans*-**9**, and the spectrum is interpreted on this basis. The assignment must

Table 2. ^{13}C-NMR Spectral Data for Halophenylphosphetane Oxides[a]

Compound	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15
trans-**4**	50.2	30.8	37.2	16.5	23.3	14.7	–	–	129.1	132.1	129.1	138.6		
	(64.5)	(12.1)	(52.4)	(4)[b]	(2.7)	(29.5)	–	–	(77.3)	(10.7)	(11.0)	(0)		
trans-**5**	46.9	45.0	46.9	18.7	23.9	7.3	18.7	23.9	–[b]	133.7	128.3	138.1		
	(58.2)	(6.6)	(58.2)	(4.4)	(3.3)	(18.2)	(4.4)	(3.3)		(9.9)	(11.0)	(4.4)		
cis-**5**	46.0	45.0	46.0	19.7	24.0	7.6	19.7	24.0	–[b]	133.1	128.4	138.1		
	(58.2)	(6.6)	(58.2)	(~1)	(4.4)	(16.5)	(~1)	(4.4)		(9.9)	(9.9)	(3.3)		
trans-**6**	49.3	30.0	36.5	15.8	22.7	14.0	–	–	125.8	132.5	115.5	163.8		
	(63.7)	(12.1)	(52.8)	(4.4)	(4.4)	(29.7)	–	–	(70.3)	(11.0)	(12.1)	(–[c])		
									[–[c]]	[8.8]	[20.9]	[24.6]		
trans-**7**[c]	46.8	45.2	46.8	18.8	24.2	7.4	18.8	24.2	–[b]	–[b]	–[b]	–[b]		
	(58.1)	(5.5)	(58.1)	(4.9)	(2.2)	(23.6)	(4.9)	(2.2)						
cis-**7**	46.1	45.7	46.1	19.9	24.1	8.2	19.9	24.1	–[b]	–[b]	–[b]	–[b]		
	(59.3)	(–[b])	(59.3)	(~1)	(3.3)	(16.5)	(~1)	(3.3)						
trans-**8**	47.9	45.1	47.9	18.6	23.9	7.6	18.6	23.9	128.1	133.0	131.1	136.3	134.3	130.0
	(58.2)	(5.5)	(58.2)	(4.4)	(3.3)	(28.1)	(4.4)	(3.3)	(55.1)	(13.2)	(8.8)	(0)	(9.9)	(11.0)
trans-**9**	50.8	29.6	39.9	16.0	23.5	14.3	–	–	128.3	132.5	127.0	138.9	130.7	138.7
	(63.1)	(10.8)	(55.1)	(2.7)	(4.0)	(28.2)	–	–	(65.8)	(10.7)	(9.4)	(0)	(6.7)	(6.7)

[a] For numbering, see structures **8** and **9**. Chemical shifts are ppm downfield from TMS. Values in parentheses are J_{PC} (Hz); values in brackets are J_{FC} (Hz). Samples of **4**, **6**, **8**, and **9** exceeded 90% trans isomer, as determined by ^{31}P-NMR spectroscopy. Samples of **5** and **7** were about 60–70% trans isomer, as determined by ^{31}P-NMR spectroscopy.
[b] Not measured.
[c] Spectrum reported in Ref. 6.

however be considered tentative at this time. With *p*-dichlorobenzene, no reaction occurred with PCl_3-AlCl_3 under the conditions used, but more forcing conditions could well give different results.

Since a variety of aromatic compounds can participate in the PCl_3-AlCl_3 reaction,[4] it is probable that a considerable number of new arylphosphetane oxides can be made by this basically one-step process.

^{1}H-NMR spectra were obtained on an IBM NR-80 spectrometer, using tetramethylsilane as internal standard. ^{31}P-NMR FT spectra were obtained on a JEOL FX-90Q spectrometer at 36.2 MHz, using 85% phosphoric acid as external standard with an internal deuterium lock. Positive shifts are downfield of the reference. ^{13}C-NMR spectra (FT) were obtained on the same instrument at 22.5 MHz with tetramethylsilane as internal standard. Broad-band noise-decoupling was employed on all ^{13}C and ^{31}P spectra. Melting points were taken on a Mel-Temp apparatus and are corrected. Microanalyses were performed by MHW Laboratories, Phoenix, Arizona.

1-(*p*-Fluorophenyl)-2,2,3-trimethylphosphetane 1-oxide (6); Typical Procedure:

A mixture of anhydrous aluminum chloride (13.3 g, 0.10 mol) and fluorobenzene (9.6 g, 0.10 mol) in phosphorus trichloride (26 ml) is stirred at reflux for 3 h. The hydrogen chloride evolved is trapped by passage over water. The flask is then fitted for vacuum distillation, and the excess phosphorus trichloride is removed as completely as possible with a water aspirator. Dry dichloromethane (100 ml) is added, and while the mixture is being stirred in an ice-salt bath, 3,3-dimethyl-1-butene (8.4 g, 0.10 mol) is added dropwise. The mixture is then stirred at room temperature for 20 h. Hydrolysis is accomplished by the addition of ice-cold water (100 ml), with the flask cooled in an ice-water bath so as to keep the temperature below 10 °C. The organic layer is separated and washed with cold 5% sodium hydrogen carbonate (100 ml), and then with water (2 × 50 ml). The water layer from the hydrolysis is extracted with dichloromethane, and the combined dichloromethane phase is dried with sodium sulfate. Removal of solvent by rotary evaporation leaves a colorless oil that is distilled by the Kugelrohr technique at 120–122 °C (1.2 torr). The crude product (14.9 g) solidifies on standing. Other data are provided in Tables 1 and 2. Chromatography on silica gel with elution by hexane/ethyl acetate is effective in increasing the *trans* content (> 90%).

1-(p-Chlorophenyl)-2,2,3-trimethylphosphetane 1-oxide **(4)** is prepared by the same procedure; data are given in Tables 1 and 2.

For *phenyl-2,2,3-trimethylphosphetane 1-oxide* **(2)**, the reflux period in the benzene-phosphorus trichloride-aluminum chloride reaction is 18 h. The yield of recrystallized *trans* **2**, containing variable but small amounts of *cis* **2**, is 80%.

The yields of *cis* isomers can be increased, if desired, by pouring the reaction mixture onto crushed ice in the hydrolysis step.

1-Aryl-2,2,3,4,4-pentamethylphosphetane 1-Oxides; General Procedure:

The use of 2,4,4-trimethyl-2-pentene in the same procedure as described above leads to the synthesis of the 1-phenyl- **(3)**, 1-(*p*-chlorophenyl)- **(5)**, 1-(*p*-fluorophenyl)- **(7)**, and 1-(3,4-dichlorophenyl)- **(8)** derivatives of 2,2,3,4,4-pentamethylphosphetane 1-oxide (Tables 1 and 2). In the synthesis of **3** and **8**, the reflux period in the reaction is 18 h. All of these products generally crystallized after solvent stripping, and are not distilled before recrystallization. Samples can be enriched in *trans* isomers by column chromatography.

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