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Almaz Zagidullin^a, Yulia Ganushevich^a, Vasili Miluykov^a, Oleg Sinyashin^a & Evamarie Hey-Hawkins^b

^a A. E. Arbuzov Institute of Organic and Physical Chemistry of the Russian Academy of Sciences, Arbuzov Str., 8, 420088, Kazan, Russia

^b Institut für Anorganische Chemie, Universität Leipzig, Johannisallee 29, 04103, Leipzig, Germany

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Versatile cycloaddition reactions of 1-alkyl-1,2-diphospholes

Almaz Zagidullin,^{1*} Yulia Ganushevich,¹ Vasili Miluykov,¹ Oleg Sinyashin¹ and Evamarie Hey-Hawkins²

¹A. E. Arbuzov Institute of Organic and Physical Chemistry of the Russian Academy of Sciences, Arbuzov Str., 8, 420088 Kazan, Russia. E-mail: <u>zagidullin@iopc.ru</u>; Fax: +7-843-273-18-72 ²Institut für Anorganische Chemie, Universität Leipzig, Johannisallee 29, 04103 Leipzig, Germany

Abstract Reactivity of 1-alkyl-1,2-diphospholes in cycloaddition reactions with dienes, dienophiles or 1,3-dipoles was examined. 1-Alkyl-1,2-diphospholes (**2**) exhibit dual reactivity and act as diene toward maleic acid derivatives or dienophiles with 2,3-dimethyl-1,3-butadiene. The 1-alkenyl-1,2-diphospholes (**4**) are readily involved into intramolecular [4+2] cycloaddition reactions leading to cage phosphines (**5**). Interaction of 1-alkyl-1,2-diphospholes (**2**) with 1,3-dipolar reagents (diphenyldiazomethane and nitrones) results formation of the bicyclic phosphiranes (**8**) and dimers of 1-alkyl-1,2-diphosphole oxides (**9**) or bicyclic phosphine oxides (**10**) with β -lactam moiety depending on temperature.

Keywords polycyclic phosphines; 1-alkyl-1,2-diphospholes; cycloaddition reactions; phosphorus heterocycles

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Polycyclic and cage phosphines on the basis of the phosphanorbornene and phosphanorbornadiene framework are regarded as weak, highly space filling ligands with a bridgehead non-racemizable chiral phosphorus center in homogeneous, biphasic and asymmetric catalysis. Representative examples of polycyclic phosphorus compounds are provided by PennPhos^[i], BIPNOR^[ii], NORBOS^[iii], phosphanorbornadiene diimines^[iv], trycyclic phosphinites^[v], P₅-deltacyclenes^[vi], which have been successfully used as enantiopure ligands for asymmetric catalysis. This phosphines are competitive with the best ligands proposed in the literature in terms of both activity and enantioselectivity^{[vii], [viii]}.

From a synthetic standpoint, such polycyclic phosphines are readily accessible via cycloaddition reactions of phospholes with different alkenes and alkynes. Most studied are cycloaddition reactions of two tautomeric forms of monophospholes - 1*H*- and 2*H*-phospholes^[ix]. Typically 1*H*-phospholes are thermally stable and act rather as poor dienes toward classic dienophiles^[x] due to residual aromaticity^[xi], whereas 2*H*-phospholes are much less stable and demonstrate high activity in cycloaddition reactions^[xii]. In this manner are of special interest the 1-alkyl-1,2-diphosphacyclopenta-2,4-dienes (1-alkyl-1,2-diphospholes) (**2**) combining structural elements both of 1*H*- and 2*H*-phospholes. Herein we will summarize our results in the field of cycloaddition reactions of 1-alkyl-1,2-diphospholes with different dienes, dienophiles and 1,3-dipolar reagents.



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The 1-alkyl-1,2-diphospholes (**2**) are readily available by alkylation of sodium 3,4,5triphenyl-1,2-diphosphacyclopentadienide (**1**) with alkyl bromides or iodides (scheme 1)^[xiii]. Surprisingly, the 1-alkyl-1,2-diphospholes (**2**) reveal a great thermal stability like 1*H*-phospholes - dimerization reaction of (**2**) was observed only at heating up to 190° C leading to the tricyclic product (**3**) of [2+2] cycloaddition reaction of 1,2-diphospholes^[xiv] formed by R[1,5]-shift of alkyl group.

At the same time stability of 1-alkenyl-1,2-diphospholes (**4**) obtained by alkylation of sodium 3,4,5-triaryl-1,2-diphosphacyclopentadienide (**1**) with $Br(CH_2)_nCH=CH_2$ depends on the length of alkyl chain (scheme 1). Thus, (**1**) reacts with allyl bromide or 6-bromo-1-hexene to give the corresponding 1-alkenyl-1,2-diphospholes (**4a**, **d**) which undergo [4+2] intermolecular cycloaddition reactions to form polymeric compounds. However, alkylation of (**1**) with 4-bromo-1-butene or 5-bromo-1-pentene proceeds highly regioselectively with the formation of cage phosphines (**5b**, **c**) in 75-80% yields at room temperature, which are the products of intramolecular [4+2] cycloaddition reactions of corresponding 1-alkenyl-1,2-diphospholes (**4b**, **c**)^[xv]. It should be noted that the intramolecular [4+2] cycloaddition reaction of 1-butenylphosphole proceed with moderate yield only at heating up to 160°C in xylene for 10–12 $h^{[xvi]}$. Thus 1-alkyl-1,2-diphospoles (**1**) seems to be an analogue both *1H*- and *2H*-phospholes.

Indeed 1-alkyl-1,2-diphospholes (**2**) react with maleic acid derivatives in mild conditions to give the corresponding [4+2] cycloaddition products (**6**) in 80-95% yields (scheme 2). Only *anti-endo*-isomer of 1.7-diphosphanorbornene against 4 possible was formed. It should be noted that the similar [4+2] cycloaddition reaction for 1,2,5-triphenylphosphole with maleic acid

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derivatives proceed at elevated temperatures with low yields (3-11%) and forming of mixture of two isomers^[xvii].

Moreover as stable analogues of 2*H*-phospholes, 1-alkyl-1,2-diphospholes (**2**) exhibit dual reactivity and can also act as dienophiles. Thus, 1,2-diphospholes (**2**) react with 2,3-dimethylbutadiene-1,3 at room temperature to give 9-alkyl-3,4-dimethyl-6,7,8-triphenyl-1,9-diphosphabicyclo[4.3.0]nona-3,7-dienes (7) in 80 % yields^[xviii].

At the same time, 1,3-dipolar cycloaddition reactions of monophospholes have been poorly studied in contrast to their Diels–Alder reactions^[xix]. Therefore, it was interesting to study the reactivity of 1-alkyl-1,2-diphospholes (**2**) toward different 1,3-dipoles – diphenyldiazomethane and nitrones. We have found that 1-alkyl-1,2-diphospholes (**2**) react with diphenyldiazomethane cleanly at room temperature to form 2-alkyl-3,4,5,6,6-pentaphenyl-1,2diphosphabicyclo-[3.1.0]hex-3-enes dienes (**8**) in 70-75 % yields.

While 1-alkyl-1,2-diphospholes (2) demonstrate similar behavior in reactions with diphenyldiazomethane like other heterophospholes^[19], reactions of (2) with nitrones are more complicated. At room temperature only dimer of 1-alkyl-1-oxo-1,2-diphospholes (9) are obtained in 70-80% yield. Probably nitrones act as mild oxidant leading to unstable oxides of 1-alkyl-1,2-diphospholes, which immediately undergo [4+2] cycloaddition reactions to yield compounds (9). However at elevated temperature reaction of (2) with nitrones lead to bicyclic phosphine oxides (10) with β -lactam moiety. Formation of (10) takes place also in an independent reaction of (9) with nitrones^[xx].

In summary, we have demonstrated that 1-alkyl-1,2-diphospholes combine the properties of both *1H*-phospholes (thermal stability) and *2H*-phospholes (high and dual reactivity in

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cycloaddition reaction). Bi-, tricyclic and cage phosphines **5-9** are accessible in high yields (75-95%) as pairs of enantiomers. This reactions proceed in mild conditions (25°C, 6-12h) with high regio- and stereoselectivity, which open new possibilities to construct new chiral polycyclic phosphines with chiral bridgehead phosphorus atoms for asymmetric catalysis^{[2], [7]}.



Scheme 1. Synthesis and thermal stability of 1-alkyl-1,2-diphospholes.

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Scheme 2. Reactivity of 1-alkyl-1,2-diphospholes toward dienes, dienophiles and 1,3-dipolar

reagents.

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