Organophosphorus compounds based on 1,4- and 1,5-diketones*

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The phosphorylation reactions of 1,4- and 1,5-diketones with dimethyl phosphites, hypophosphorous acid and its esters, and phosphines are discussed. The reactions lead usually to the formation of cyclic compounds.

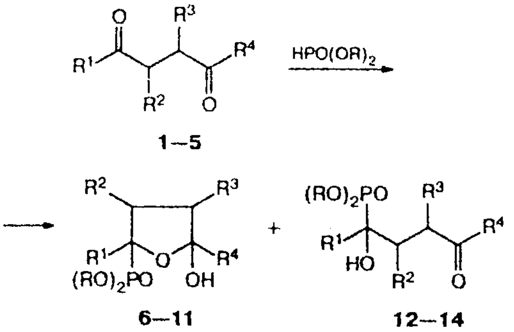
Key words: 1,4-diketones, 1,5-diketones, phospholanes, phosphorinanes, phosphinic acids, phosphonic acids, tetrahydrofurans, tetrahydropyrans.

1,4- and 1,5-Diketones are convenient starting compounds for the synthesis of cyclic systems. Various nitrogen-, sulfur-, and oxygen-containing heterocycles and carbocyclic compounds were synthesized from them; however, these substrates have not attracted the attention of organophosphorus chemists for a long time. In seventies, in Far Eastern State University, we began work on phosphorylation of 1,5-diketones and later, 1,4-diketones.

Phosphorylation of 1,4- and 1,5-diketones by H_3PO_3 derivatives

Reactions with dialkyl phosphites. Primarily, the reaction of 1,4-diketones with dialkyl phosphites was studied for 2,5-hexanedione.[1,2] It is shown that under conditions of base catalysis, two molecules of dialkyl phosphite add to both carbonyl groups of the diketone to form acyclic products. Under these conditions, more complex 1,4-diketones **1—5** add one dialkyl phosphite molecule (R = Me, Et) and form cyclic hemiacetals **6—11** and their linear isomers **12—14** [3] (Scheme 1).

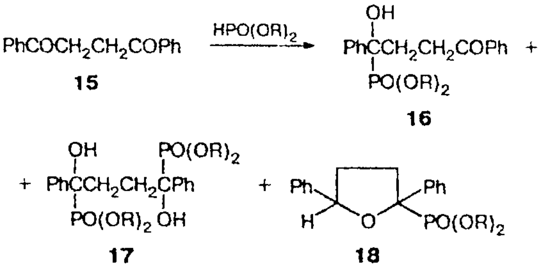
Scheme 1



	R^1	R^2	R^3	R^4
1, 6, 7	$(CH_2)_4$	$(CH_2)_4$	$(CH_2)_4$	$(CH_2)_4$
2, 8, 12, 13	$(CH_2)_4$	$(CH_2)_4$	H	Ph
3, 9, 14	$(CH_2)_3$	$(CH_2)_3$	H	Ph
4, 10	$(CH_2)_3$	$(CH_2)_3$	H	Bu^t
5, 11	$(CH_2)_3$	$(CH_2)_3$	H	Me

Under these conditions, arylaliphatic 1,4-diketone **15** form compounds **16—18** [3] (Scheme 2).

Scheme 2



Compounds **18** were most likely formed due to the reduction of intermediate acetals similar to compounds **6—11**.

1,5-Diketones react with dimethyl phosphite to give compounds with somewhat different structure.[4] In the presence of sodium methoxide (1 equiv.), diketone **19** with dimethyl phosphite forms compound **20**; and compound **21** is formed in the presence of an excess of alkali (Scheme 3).

This result can be explained as follows. The dimethyl phosphite anion adds to one of the carbonyl groups of diketone **19** to form alkoxide anion **A**. Then the cyclization (through the stage of ion **B**) to tricyclic molecule **20** occurs. Similar transformations are presently known as

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* Dedicated to the memory of Academician M. I. Kabachnik on his 90th birthday.

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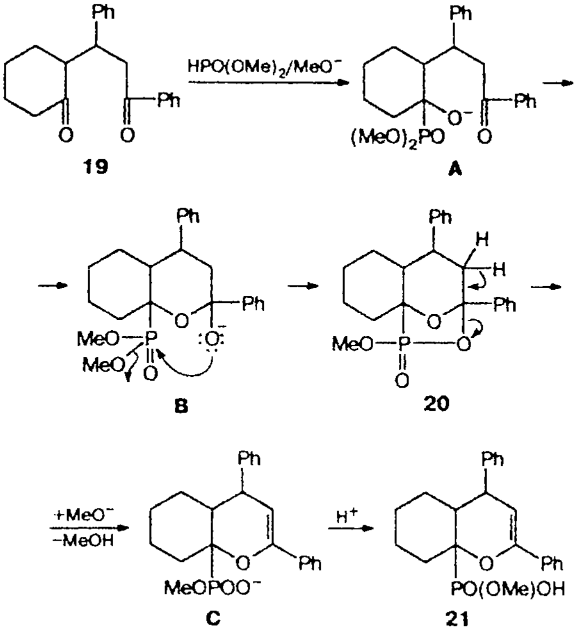
Scheme 3



domino reactions[5] or cascade processes.[6] Under the action of an excess of sodium methoxide, a proton is eliminated, and anion **C** is formed, which can be further transformed by acidification into compound **21**.

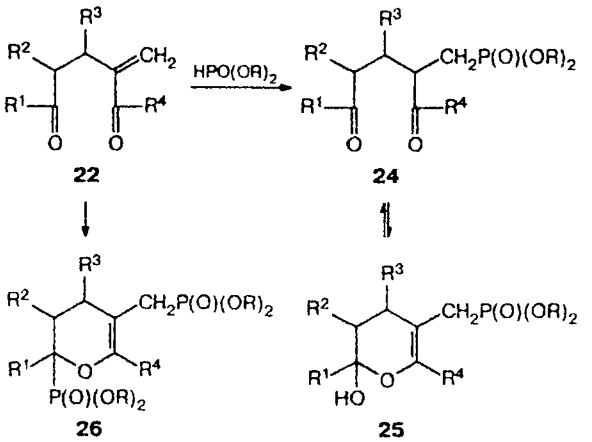
Other 1,4-diketones react similarly.[4] The *cis*-diaxial arrangement of the phosphonate group and O$^-$ in intermediate **B** is the necessary condition for this process. Perhaps, in compounds **6—11**, the phosphonate and hydroxyl groups are in the *trans*-position and, hence, no cyclization occurs.

2-Methylene-1,5-diketones and 2,4-dimethylene-1,5-diketones in the reactions with dimethyl phosphites. The easily accessible 2-methylene-1,5-diketones (**22**) and 2,4-dimethylene-1,5-diketones (**23**) represent one more type of substrates appropriate for the synthesis of various cyclic organophosphorus compounds. The reaction of compounds **22** with dimethyl phosphite affords three types of compounds: the Michael adduct **24**, its tautomeric hemiacetal **25**, and the product of bis-phosphorylation **26** [7,8] (Scheme 4).

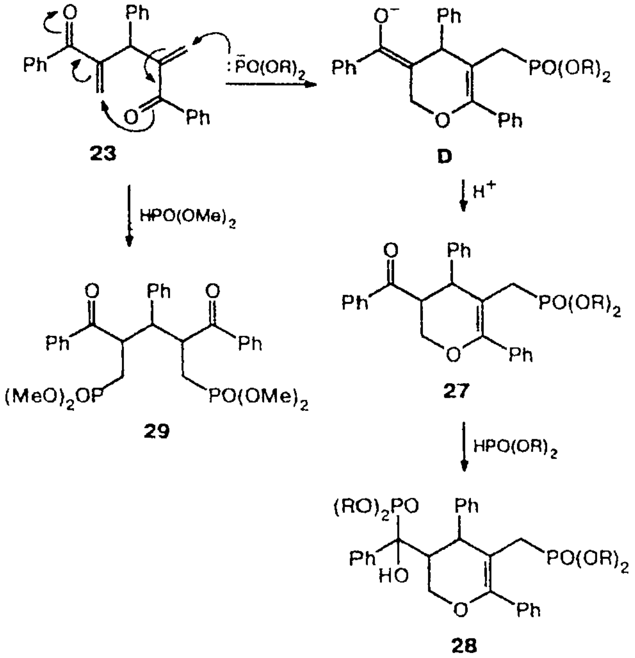
The reactions of 2-methylene-1,5-diketones with dibutylphosphinic acid occur similarly.[9]

Dimethylenediketone **23** with dimethyl and diethyl phosphites forms compounds **27—29** [8] (Scheme 5). Compounds **27** and **28** are the main products, and the latter is most likely produced on addition of dialkyl phosphite to compound **27**. In turn, dihydropyran **27** is formed due to a cascade of additions of a nucleophile to a molecule of the starting dimethylenediketone through intermediate **D**. The "normal" addition product **29** was isolated in an insignificant yield only in the reaction with dimethyl phosphite.

Scheme 4

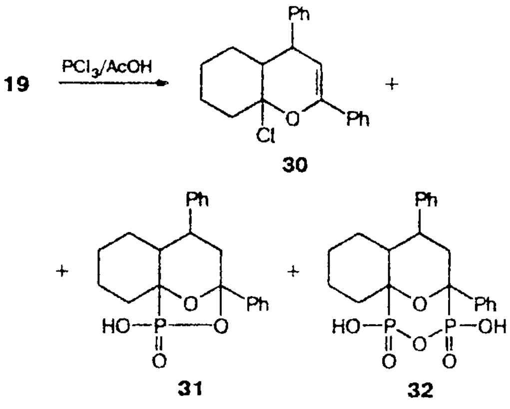


Scheme 5



The reaction with phosphorus trichloride[10,11] in acetic acid was studied in most detail for diketone **19**. After mixing of the components at room temperature, crystals of chloride **30** precipitate rapidly from the reaction mixture. If the reaction is not interrupted at this moment, the crystals are dissolved, and compound **31** is formed. The reaction at 65 °C results in the formation of anhydride **32** (Scheme 6). The formation of similar compounds was also observed in the reactions of 1,5-diketones with methyldichlorophosphine[12].

Scheme 6



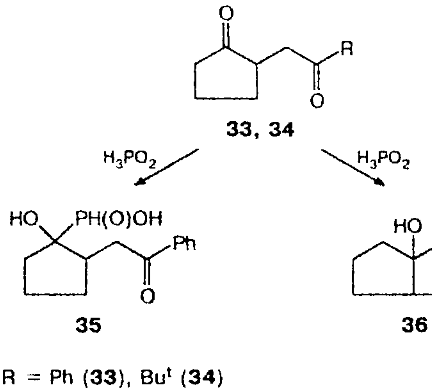
Phosphorylation of 1,4- and 1,5-diketones by H_3PO_2 and its derivatives

Reaction with hypophosphorous acid. It is known that H_3PO_2 can add to one or two molecules of a carbonyl compound to form mono- or disubstituted phosphinic acids.[13,14]

$$RR'C=O + H_3PO_2 \longrightarrow$$
$$\longrightarrow RR'C(OH)PO(H)OH + [RR'C(OH)]_2P(O)OH$$

1,4-Diketones react with hypophosphorous acid according to this scheme.[15] Diketone **33** adds H_3PO_2 to one of the carbonyl groups only (adduct **35**), whereas the more reactive diketone **34** is transformed into phospholane **36** (Scheme 7).

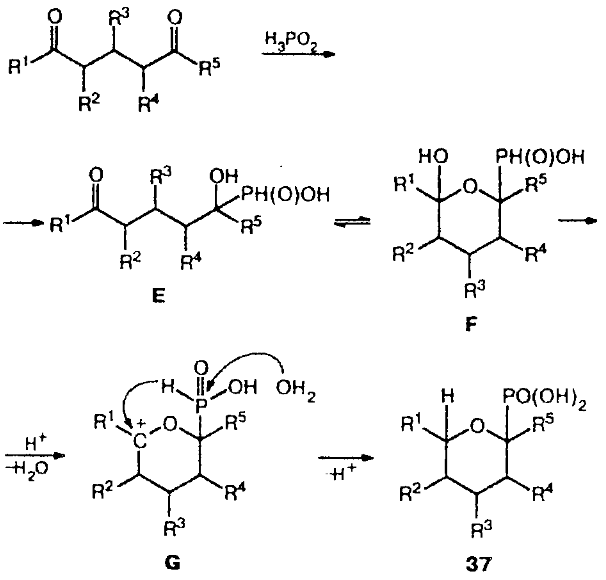
Scheme 7



R = Ph (**33**), Bu^t (**34**)

1,5-Diketones react in a different way.[16,17] Arylaliphatic diketones in acetic acid and "semicyclic"[18] diketones in dioxane are transformed under the action of hypophosphorous acid into tetrahydropyranyl-2-phosphonic acids (**37**) (Scheme 8).

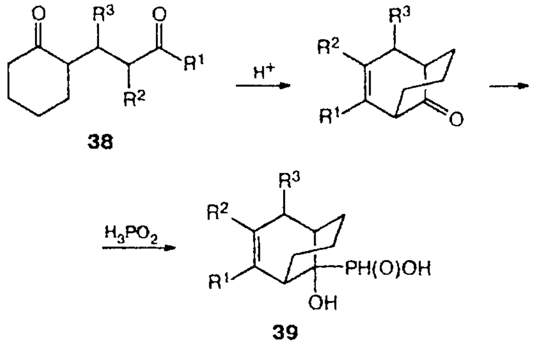
Scheme 8



This result can be explained by the fact that adduct **E** that is primarily formed can be reversibly cyclized to tetrahydropyranol **F**, which loses water in an acidic medium. The hydride shift of hydrogen from the phosphorus atom to the carbocation and hydration of the phosphorus atom occur in ion **G** that is formed as an intermediate. This scheme is confirmed by the transformation of authentic compounds with structure **E** upon heating with acetic acid into compounds **37**.[19,20]

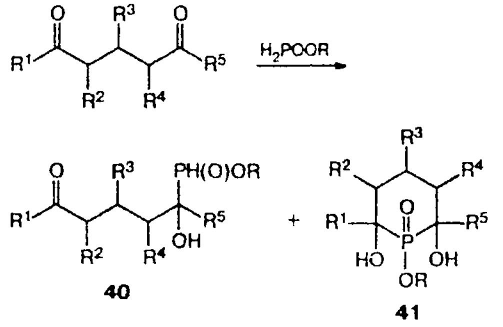
1,5-Diketones with the methylene group in position 6 to carbonyl can be cyclized under the action of acids to cyclohexenones. Therefore, diketones of type **38** heated with H_3PO_2 in acetic acid form phosphinic acids **39** [21] (Scheme 9).

Scheme 9



The reaction of 1,5-diketones with alkyl hypophosphites resulted either in the formation of the product of addition to only one of the carbonyl groups (compound **40**) or in phosphorinanes **41** [19] (Scheme 10).

Scheme 10



This reaction is inconvenient from the synthetic viewpoint, since alkyl hypophosphites are unstable and have a low reactivity.

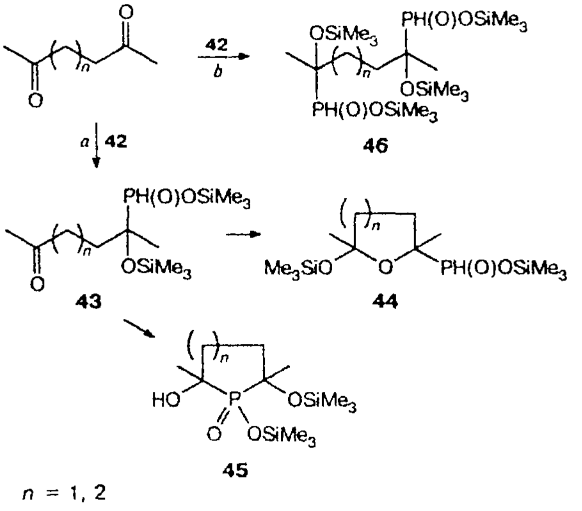
Reaction with bis(trimethylsilyl) phosphonite, $HP(OSiMe_3)_2$ 42.[22–25] Compound **42** is a derivative of the tautomeric form of hypophosphorous acid $HP(OH)_2$. The tricoordinated phosphorus in a molecule of **42** is a reactive nucleophile, and its reactions with carbonyl groups occur rapidly and in the absence of catalysts.[26] This compound is easily accessible[27] and convenient.

The result of the reaction of 1,4- and 1,5-diketones with reagent **42** is determined, in many respects, by the structure of the starting diketone. The reaction occurs *via* two main directions.

a. Diketone adds one molecule of the reagent. The primary adduct **43** can further undergo cyclization to form oxygen (tetrahydrofuran or tetrahydropyran) **44** or phosphorus (phospholane or phosphorinane) **45** heterocycles. The latter direction of the reaction was discussed in Ref. 28.

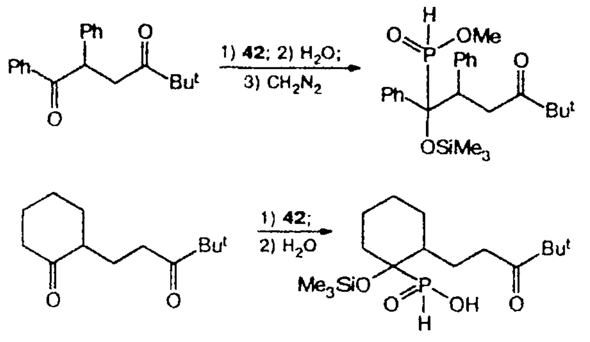
b. Diketone adds two molecules of the reagent to form bis-phosphinates **46**.

Scheme 11



The reaction ceases at the stage of compounds **43** if one of the carbonyl groups of diketone is shielded, for example, by the *tert*-butyl substituent (Scheme 12):[20,23]

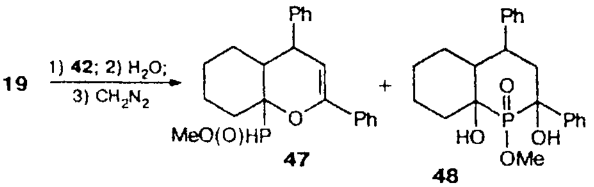
Scheme 12



When both carbonyls are accessible, cyclization occurs, which is favored by the presence of the phenyl group at the C(2) atom (in a molecule of 1,4-diketone) or C(3) (in 1,5-diketone). The addition of the second molecule of the reagent is alternative to this route.

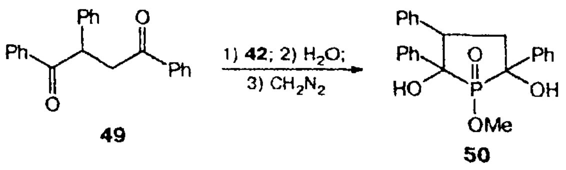
1,5-Diketone **19** adds reagent **42** to form hydrochromene **47** and phosphorinane **48** (Scheme 13).

Scheme 13



1,2,4-Triphenyl-1,4-butanedione (**49**) with reagent **42** forms phospholane **50** (Scheme 14).

Scheme 14

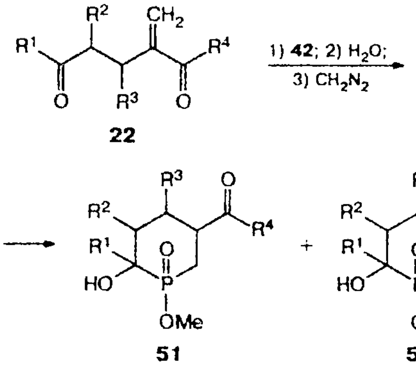


Hydroxyl groups at the C(2) and C(5) atoms of dihydroxyphospholanes are arranged in *trans*-positions, whereas hydroxyls at the C(2) and C(6) atoms in dihydroxyphosphorinane molecules occupy *cis*-diaxial positions.

1,2-Dibenzoylethane adds two molecules of reagent **42**.

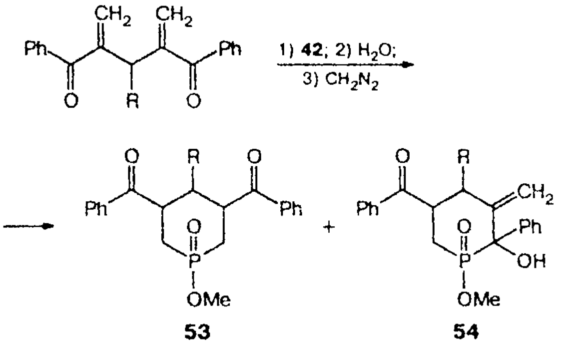
*2-Methylene-1,5-diketones and 2,4-dimethylene-1,5-diketones in reactions with bis(trimethylsilyl) phosphonite **42**.* 2-Methylene-1,5-diketones **22** mainly form products of addition to the conjugated C=C—C=O system and to nonconjugated carbonyl group **51**; compounds **52**, which have not been observed previously in similar reactions,[29,30] were obtained as minor products (Scheme 15).

Scheme 15



Dimethylenediketones add reagent **42** mainly to both conjugated C=C—C=O systems (compounds **53**); however, in this case, unsaturated phosphorinanes **54** were obtained in a low yield[31,32] (Scheme 16).

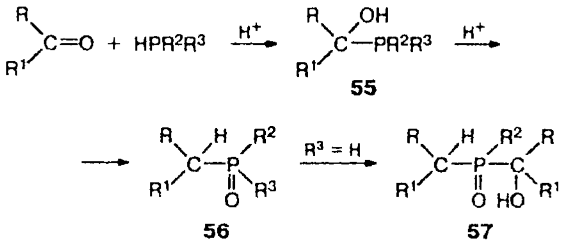
Scheme 16



Phosphorylation of 1,4- and 1,5-diketones by phosphines

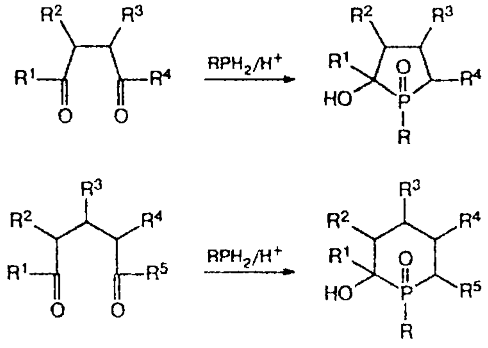
The reaction of phosphines with ketones was considered in the papers published previously.[33—35] Phosphine and primary and secondary phosphines react with ketones in a strongly acidic medium. The primary product of addition, hydroxyphosphine **55**, is rearranged under the action of acids into phosphine oxide **56**. In the case where at least one H atom is present at phosphorus in a molecule of **56**, the second ketone molecule adds to form compound **57** (Scheme 17).

Scheme 17



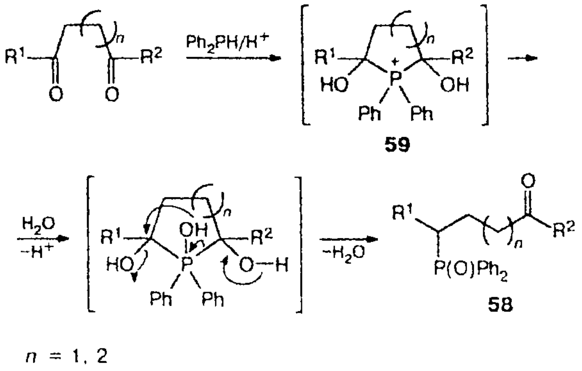
The reactions of 1,4- and 1,5-diketones with phosphine and phenylphosphine occur according to this scheme and result in the formation of 2-hydroxyphospholanes[36,37] and 2-hydroxyphosphorinanes,[38—40] respectively (Scheme 18).

Scheme 18



Oxo-phosphine oxides **58** are formed in the reactions of diphenylphosphine with 1,4- and 1,5-diketones regardless of molar ratios of the reagents[41,42] (Scheme 19).

Scheme 19



coordinated phosphorus when the pH of the mixture changes.

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