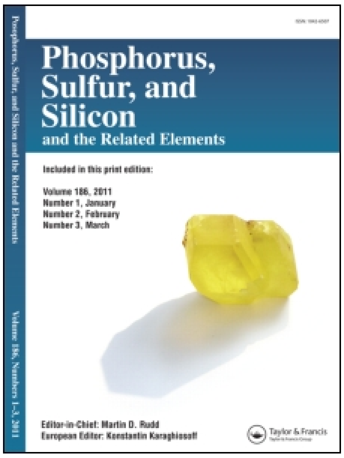

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INSERTION OF CARBENES INTO P—H BONDS. 5. SYNTHESIS OF NEW PHOSPHONATES AND PHOSPHINATES IN REACTIONS CATALYSED BY Cu,Pd,Rh,Ni COMPLEXES

Alexander M. Polozov[a]; Albert H. Mustaphin[a]; Alexander V. Khotinen[a]
[a] A. M. Butlerov Scientific Research Chemical Institute, Kazan State University, Kazan, Russia

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INSERTION OF CARBENES INTO P—H BONDS. 5.† SYNTHESIS OF NEW PHOSPHONATES AND PHOSPHINATES IN REACTIONS CATALYSED BY Cu,Pd,Rh,Ni COMPLEXES

ALEXANDER M. POLOZOV,* ALBERT H. MUSTAPHIN and
ALEXANDER V. KHOTINEN
A. M. Butlerov Scientific Research Chemical Institute, Kazan State University,
Lenin Str., 18, Kazan, 420008, Russia

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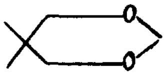
$Cu(OTf)_2$ and $Cu(acac)_2$ were found to be the most effective catalysts in the reaction of diazo compounds Ph_2CN_2 (**1a**), $EtOC(O)CHN_2$ (**1b**), $MeOC(O)CHN_2$ (**1c**), $MeC(O)CN_2C(O)OMe$ (**1d**), $ClCH_2C(O)CHN_2$ (**1e**) and CH_2N_2 (**1f**) with hydrophosphoryl compounds $(MeO)_2P(O)H$ (**2a**), $(t\text{-}BuO)_2P(O)H$ (**2b**), $Ph(MeO)P(O)H$ (**2c**), $(EtO)_2P(O)H$ (**2d**) and


P(O)H (**2e**)

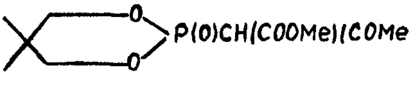
resulting in P—C bond formations. Cu, Pd and Rh acetates and $Ni(acac)_2$ have a much lower efficiency. Chlorines in $Cl_3CC(O)CH_2P(O)(OMe)_2$ (**3k**) and $Cl_2CHC(O)CH_2P(O)(OMe)_2$ (**3l**) are reduced in the copper catalysed Atherton-Todd reaction.

Key words: Catalyst; diazo compound; hydrophosphoryl compound; insertion; phosphonate; phosphinate.

INTRODUCTION

Synthesis of carbon-phosphorus bonds is a useful stage in organophosphorus chemistry.[1] Numerous reactions are known, the Arbuzov and Michaelis-Becker reactions being supplemented with several new routes.[1–4] However, all of these are rather limited. In a previous paper,[5,6] we reported that the reaction of diazo compounds with dialkyl hydrogen phosphites under catalysis by $Cu(acac)_2$ complemented the existing methods, in particular in the synthesis of 2-dialkoxyphosphonyl-1,3-dicarbonyl compounds.

To establish the potentialities inherent in this reaction, we carried out the synthesis of well-known compounds with phosphorus bearing such usual substituents as MeO, EtO, $MeOOCH_2$, Ph_2CH and Me. Furthermore, we chose previously only scarcely used phosphonates bearing t-BuO, $Cl_2CHCOCH_2$, (MeOOC)(MeCO)CH substituents for synthetic challenge. The greatest value of the phosphonate $(t\text{-}BuO)_2POCH_2COOMe$ consists in the possibility of utilization as trans stereospecific Horner-Wadsworth-Emmons reagent,[7] and of the phosphonate



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†For Part 4, see Reference 6.

as the same reagent,[8] and as model compounds for investigation of the interrelation between keto-enol and conformational equilibriums.[9]

The discovery of exceptionally effective catalysts like $Cu(OTf)_2$, $Pd(OAc)_2$ and $Rh_2(OAc)_4$[10–14] resulted in a dramatic improvement in the synthetic application for typical cyclopropanation and carbenoid insertion reactions. We have analyzed the synthetic applicability of various transition metal complexes in the catalytic insertion reaction into the P—H bond.

RESULTS AND DISCUSSION

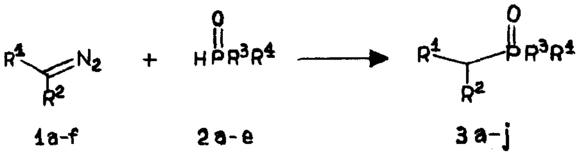
All reactions (except for **1f**) were performed under identical conditions: a benzene solution of the diazo compound was slowly added over 2–3 h (only diphenyldiazomethane(**1a**) was added in a 1 h period in order to maximize the yields of products **3a–c**) to a stirred refluxing solution of catalyst and hydrophosphoryl compound in benzene. In the case of **1f**, diethyl ether and room temperature were used (Table I).

The acyclic hydrophosphoryl compound, diazo compound, catalyst ratios were 5:1:0.03 in the case of the synthesis of **3a,c,d,e,i**. In the case of the expensive **2e**, one equivalent of this was used and the catalyst was added in 8 proportions during the reaction. The optimum catalyst content was studied for the preparation of products (**3b,e,g**) (Table II). It was found to be 10 mol % for the preparation of product (**3b**) and 3 mol % for that of the products (**3e,g**). Then, we used 10 mol % of catalyst for reactions of **2b**, and the same manner of addition of the catalyst as for **2e**. Product (**3g**) was also obtained without catalyst. It may be due to the higher acidity of phosphorinane (**2e**) compared with that of other hydrophosphoryl compounds used. The dimethyl hydrogen phosphite (**2a**), diazo methane (**1f**) ratio was 1:2.

$Cu(OTf)_2$ was found to be the most effective catalyst in the reactions of phosphorinane (**2e**) with (**1c,d**), and phosphite (**2a**) with diazomethanes (**1a,f**). However, it was relatively ineffective in other reactions. In these cases we have found that $Cu(acac)_2$ has greater potential (yields obtained with the best conditions are listed in Table I).

For comparison purposes, catalyst activities were obtained in the reaction of diazoester (**1b**) with diethyl hydrogen phosphite (**2d**) (Table III).

Rh, Pd and Ni catalysts were relatively ineffective. Suprisingly, the use of a well-known catalyst for diazoester cyclopropanation and C—H insertion[10] like $Rh_2(OAc)_4$, gave **3d** in significantly lower yield. It is a consequence of the inhibition of $Rh_2(OAc)_4$ by diethyl hydrogen phosphite (**2d**), since mild conditions for the decomposition

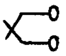
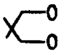


1a-f **2a-e** **3a-j**

SCHEME I

TABLE I

Organophosphorus Compounds **3a–j** Prepared

1	R^1	R^2	**2**	R^3	R^4	$\mathbf{3}^a$	Catalyst	Yield[b] (%)
a	Ph	Ph	a	MeO	MeO	a	$Cu(OTf)_2$	79
a	Ph	Ph	b	t-BuO	t-BuO	b	$Cu(acac)_2$	40
a	Ph	Ph	c	Ph	MeO	c	$Cu(acac)_2$	34
b	H	CO_2Et	d	EtO	EtO	d	$Cu(acac)_2$	83
c	H	CO_2Me	a	MeO	MeO	e	$Cu(acac)_2$	60
c	H	CO_2Me	b	t-BuO	t-BuO	f	$Cu(acac)_2$	42
c	H	CO_2Me	e			g	$Cu(OTf)_2$	40
d	COMe	CO_2Me	e			h	$Cu(OTf)_2$	37
e	H	$COCH_2Cl$	a	MeO	MeO	i	$Cu(acac)_2$	32
f	H	H	a	MeO	MeO	j	$Cu(OTf)_2$	43

[a] Phosphonates **3a,d,e,g,j** are known and their physical characteristics and NMR spectra are identical with that of the authentic samples.

[b] Yield of isolated product, based on **1**.

TABLE II

Effect of the Catalyst Content on the Yield of Dialkyl Phosphonate **3**

Dialkyl Phosphonate	Catalyst	Yield[a] (%)				
		Catalyst content[b] (mol%)				
		0	1	3	5	10
3b	$Cu(acac)_2$	0	trace	trace		40
3e	$Cu(acac)_2$	0	60			38
3g	$Cu(OTf)_2$	15	23	40	23	19

[a] Yield of isolated product, based on **1**.

[b] Based on **1**.

TABLE III

Effect of the Catalyst on the Yield of **3d**

Catalyst	Yield[a] (%)	Catalyst	Yield[a] (%)	Catalyst	Yield[a] (%)
$Cu(acac)_2$	83	$Pd(OAc)_2$	15	TfOH	2
$Cu(OTf)_2$	34	$Rh_2(OAc)_4$	10	$BF_3 \cdot OEt_2$	0
$Cu(OAc)_2$	27	$Ni(acac)_2$	trace		

[a] Yield of isolated **3d**, based on **1b**.

of the diazo ester (**1b**) in the presence of $Rh_2(OAc)_4$ (r.t. diethyl ester) proved to be unsuccessful in the presence of phosphite (**2d**) and we had to use drastic conditions (refluxing in o-xylene). Indeed, heating over a 0.5 h period $Rh_2(OAc)_4$ and **2a** at 80°C lead to an exchange reaction, which is proved by IR spectroscopic data (replacement of the ν (C═O . . . Rh) 1580 cm^{-1} to ν (COOH) 1710 cm^{-1}).

Trifluoromethanesulfonic acid (TfOH) also catalyses the reaction of **1b** with **2d**, but minor activity is observed. A higher yield of **3a** (30%) was obtained in the

TABLE IV

New Organophosphorus Compounds 3 Prepared

Product[a,b]	Mp(°C) or bp(°C)/Torr	R_f^c	n_D^{20}	^{1}H-NMR(TMS$_{int}$) δ, J(Hz)	^{31}P-NMR (H_3PO_{4ext}) δ
3b	145–146(dec) (petr.ether 30–40°C)	0.53		1.22 (s, 18H), 4.21 (d, 1H, J = 24), 6.96–7.68 (m, 10H) ($CDCl_3$)	17 (CH_2Cl_2)
3c	135–137 (cyclohexane)	0.40		3.45 (d, 3H, J = 12), 4.28 (d, 1H, J = 16.8) 6.74–7.57 (m, 15H) (CCl_4)	40 (CCl_4)
3f	100/0.09	0.54	1.4360	1.44 (s, 18H), 2.58 (d, 2H, J = 20.5), 3.47 (s, 3H) (CCl_4)	11.1 (CCl_4)
3h	101–102 (ether-$CHCl_3$)	0.52		Z-enol, 82%: 1.02 (s, 3H), 1.29 (s, 3H), 2.42 (s 3H), 3.77 (s, 3H), 4.03–4.36 (m, 4H), 13.86 (s, 1H) E-enol, 18%: 0.98 (s, 3H), 1.24 (s, 3H), 2.51 (s, 3H), 3.85 (s, 3H), 4.03–4.36 (m, 4H), 14.86 (s, 1H) ($CDCl_3$)	17.9 (Z), 13.8 (E) (toluene)
3i	97–98/0.05	0.17	1.4547	3.16 (d, 2H, J = 22), 3.72 (d, 6H, J = 11.5), 4.20 (s, 2H) (CCl_4)	17 (CCl_4)
3l		0.26		3.39 (d, 2H, J = 21), 3.72 (d, 6H, J = 11.5), 6.14 (s, 1H) (CCl_4)	14.5 (CCl_4)

[a] The IR spectra were in good accord with the proposed structures.

[b] Satisfactory microanalyses C ± 0.20, H ± 0.12, P ± 0.17.

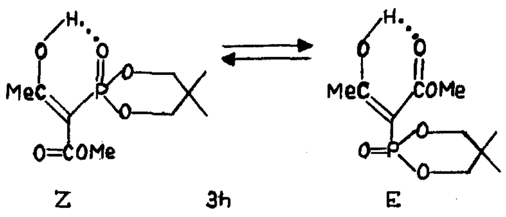
[c] Eluent - EtOAc.

reaction of diphenyldiazomethane (**1a**) with phosphite (**2a**) catalysed by the same catalyst.

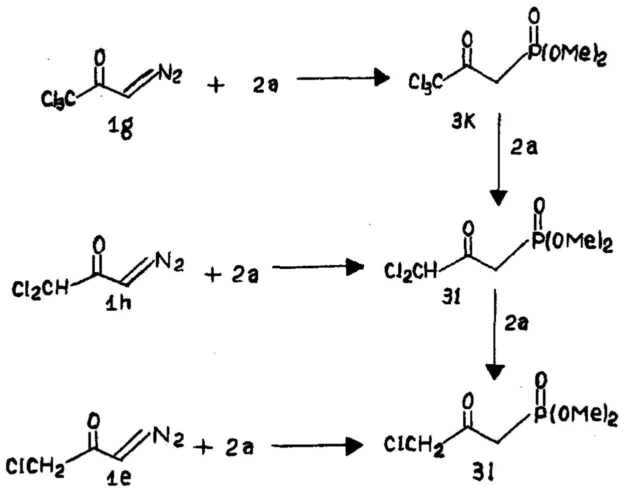
A parallel can be drawn between the activities of $Cu(OTf)_2$ and $BF_3 \cdot OEt_2$ in the Lewis acid promoted reactions of diazo compounds.[11] However, we failed to obtain **3a,d** using $BF_3 \cdot OEt_2$.

Dialkyl hydrogen phosphites (**2a,c,d**) were removed under reduced pressure and the products **3** were isolated by chromatography of the crude reaction mixture on silica gel. Compounds (**3b,c,f,h–j**) were synthesized for the first time and were characterized by ^1H, ^{31}P NMR and IR spectroscopy and satisfactory microanalyses (Table IV).

As indicated by ^1H NMR data ($CDCl_3$) phosphonate (**3h**) exists predominantly in the Z-enol form. The content of E-enol form is only 18%.



An attempt was made to apply this method for the preparation of 0,0-dimethyl-3-(di-, tri-) chloro-2-oxopropylphosphonates (**3k,l**), but we failed to obtain **3k** (Scheme II). In both reactions of **1g,h** a mixture of **3l** and **3i** was obtained. Flash chromatographic separation was accompanied by significant losses of products (**3l/3i**, 4:3 and 5:1, in the reactions of **1g** and **1h**, respectively). We believe that the chlorines are reduced in an unknown copper-catalysed Atherton-Todd reaction.[15]



SCHEME II

This assumption is supported by the reaction of methyltrichloroacetate performed under the nearly same conditions (Scheme III).

SCHEME III

In summary $Cu(OTf)_2$ and $Cu(acac)_2$ catalysed insertion of carbenes into P—H bonds compliments the existing methods of P—C bond formation, in particular in the synthesis of sterically hindered organophosphorus compounds bearing t-BuO or 1,3-dicarbonyl substituents.

EXPERIMENTAL

Reactions were performed in a dry argon atmosphere. ^{1}H NMR spectra were recorded on a Tesla-BS 467 A (60 MHz) spectrometer. ^{1}H chemical shifts were reported in ppm relative to Me_4Si as internal standard. ^{31}P spectra were recorded on a KSU-4 (8 MHz) or on a Bruker CXP 100 (36.48 MHz) spectrometer. ^{31}P chemical shifts were expressed in ppm relative to 85% H_3PO_4. IR spectra were recorded on a Specord-75 spectrometer. R_f values were obtained on plates Silufol-254 UV with EtOAc as eluent.

Benzene, diethyl ester and o-xylene were distilled from sodium benzophenon ketyl.

Quantitative separations were performed on Chemapol silica gel 100/160 (column 15/1.5 cm) and 5/40 (Flash chromatography, column 25/2 cm).

Diazo compounds (**1a–d,f**),[16] hydrophosphoryl compounds[17] and catalysts[11] were prepared according to known procedures. Diazo compounds (**1e,g,h**) were prepared by the reaction of chloroacetylchlorides with diazomethane (**1f**)[18–20] and **1e,h** were purified by chromatography on silica gel using hexane-EtOAc, 9:1, **1g** was purified by distillation at bp 62–68°C (2 Torr).

3-Chlorodiazoacetone (**1e**). Yield 60%. n_D^{20} 1.5342. ^{1}H NMR (ppm): δ 3.97 (s, 2H), δ 5.84 (s, 1H) (CCl_4). IR (cm^{-1}): ν 1720 (C=O), ν 2196 ($C{=}N_2$).

3-Trichlorodiazoacetone (**1g**). Yield 40%. n_D^{20} 1.5380. (Lit.[19]: n_D^{20} 1.5309. ^{1}H NMR (ppm): δ 5.93 (s, 1H) (CCl_4).

3-Dichlorodiazoacetone (**1h**). Yield 39%. n_D^{20} 1.5471. ^{1}H NMR (ppm): δ 5.72 (s, 1H), δ 5.79 (s, 1H) (CCl_4). IR (cm^{-1}): ν 1720 (C=O), ν 2115, ν 2180 ($C{=}N_2$).

Organophosphorus compounds (**3a–i,l**). A solution of the diazo compound **1a–e,g,h** (4 mmol) in benzene (10 ml) was added dropwise, over 2–3 h (for **1a** over 1 h), to a stirred refluxing solution of catalyst (0.13 mmol for **2a,c–e**; 0.40 mmol for **2b**; 8 equal portions were added in identical time intervals during reactions of **2b,e**) and hydrophosphoryl compound (20 mmol of **2a–d**; 4 mmol of **2e**) in benzene (10 ml). The benzene was then evaporated, excess of phosphite (**2a,c,d**) was removed under reduced pressure and the mixture was chromatographed on silica gel using hexane-benzene as eluent. The crude products (**3a–c,h**) were purified by recrystallization from the appropriate solvent, the products (**3d–g**) by distillation, the products (**3i,l**) by flash chromatography using EtOAc as eluent.

Dimethylmethylphosphonate (**3j**). A solution of the diazomethane (**1f**) (4 mmol) in diethyl ester (8 ml) was added dropwise over 2 h to a stirred solution of $Cu(OTf)_2$ (0.13 mmol) and dimethyl hydrogen phosphite (**2a**) (2 mmol) in diethyl ester (3 ml) at r.t^{0}. The solvent was then evaporated and the mixture was chromatographed on silica gel using hexane-benzene as eluent, giving product (**3j**) (Yield 43%). ^{31}P-NMR δ 34 ppm (Lit.[17]: 33.7 ppm).

Exchange reaction of $Rh_2(OAc)_4$ *with dimethyl hydrogen phosphite* (**2a**). A mixture of $Rh_2(OAc)_4$ (0.04 mmol) and phosphite (**2a**) (0.27 mmol) was stirred and heated at 80°C for 1 h. Acetic acid was identified by comparision of IR spectrum of reaction mixture with that of an authentic mixture of acetic acid and phosphite (**2a**). Reaction mixture or acetic acid + phosphite (**2a**). IR: ν 1710 cm^{-1}.

$Cu(acac)_2$ catalysed reaction of methyltrichloroacetate (**4**) *with dimethyl hydrogen phosphite* (**2a**). The mixture of methyltrichloroacetate (**4**) (4 mmol), dimethyl hydrogen phosphite (**2a**) (8 mmol) and $Cu(acac)_2$ (0.4 mmol) was heated at 100–150°C, while methyldichloroacetate (**5**) (Yield 21%) was distilled off. B.p. 90°C (100 Torr). n_D^{20} 1.4419 (Lit.[21]: n_D^{20} 1.4428). ^{1}H-NMR (ppm): δ 3.8 (s, 3H), δ 5.84 (s, 1H) (CCl_4).

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