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Microwave-assisted synthesis of α -aminophosphine oxides

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ABSTRACT

Aminophosphine oxides and bis(phosphinoylmethyl)amines were synthesized by the microwave (MW)-assisted Kabachnik-Fields reaction of primary amines, paraformaldehyde and secondary phosphine oxides. The bisphosphines obtained after deoxygenation of the bis(phosphinoymethyl)-amine derivatives were utilized in the synthesis of cyclic transition metal complexes.

GRAPHICAL ABSTRACT

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KEYWORDS

Kabachnik–Fields reaction; microwave; α-aminophosphine oxides; transition metal complexes

Introduction

 α -Aminophosphine oxides as potential precursors of α -aminophosphine ligands have attracted much attention. a--Aminophosphines are of considerable importance in the synthesis of P(III)-transition metal complexes.¹ One of the most convenient and widespread methods for the synthesis of α -aminophosphine oxides is the Kabachik-Fields, or so called phospha-Mannich reaction.²⁻⁴ This reaction is based on the condensation of an amine, an aldehyde or ketone and a > P(O)H species, such as dialkyl phosphite or secondary phosphine oxide. In case of the double Kabachnik-Fields condensations, the primary amines are reacted with two equivalents of aldehyde and two equivalents of the P-component. Since the discovery of the reaction, most of the papers were on cases utilizing dialkyl phosphites.⁵ However, there are only a few examples with secondary phosphine oxides. In this work, our recent results are summarized on the synthesis of novel aminophosphine oxides.6

Results and discussion

Synthesis of secondary phosphine oxides by Grignard reaction

As the first step of our work, the secondary phosphine oxides (dibenzyl- (1), diphenyl- (2) and bis(4-methylphenyl)phosphine oxide (3)) were prepared from diethyl phosphite by reaction with Grignard reagent, such as alkyl- or arylmagnesium bromide (Scheme 1).⁷ After purification of the crude product, the secondary phosphine oxides were obtained in yields of 84–86%.

Kabachnik-Fields reaction of secondary phosphine oxides

In the first approach, the phospha-Mannich reaction of various primary amines (propyl-, butyl-, cyclohexyl..., benzyl- or 4-methoxy-benzylamine, as well as aniline or 4-methoxyaniline) was studied with paraformaldehyde and dibenzyl- (1), diphenyl- (2) or bis(4-methylphenyl)-phosphine oxide (3) at 100 °C under MW conditions in the absence of any catalyst (Scheme 2). The condensations were performed in acetonitrile due to the heterogeneity of the reaction mixtures. After an irradiation of 1 h, the (aminomethyl)phosphine oxides (4a-f, 5a-f and 6a-f) were obtained in excellent yields (94–98%).

Double Kabachnik-Fields reaction of secondary phosphine oxides

The synthesis of bis(phosphinoylmethyl)amines (**7b-d**, **8b-d** and **9b-d**) was also studied by the double Kabachnik-Fields reaction of primary amines, two equivalents of paraformalde-hyde and two equivalents of the > P(O)H species (dibenzyl- (1), diphenyl- (2) or bis(4-methylphenyl)-phosphine oxide (3) (Scheme 3). The condensations were performed without any catalyst, and the corresponding bis(phosphinoylmethyl)amines (**7b-d**, **8b-d** and **9b-d**) were obtained in yields of 88–98%.

Kabachnik-Fields reaction of (aminomethyl)dibenzylphosphine oxide

The synthesis of nonsymmetric *N*,*N*-bis(phosphinoylmethyl)amines (**10b-d**) was carried out by the condensation of 2 👄 A. TRIPOLSZKY ET AL.

EtO
$$H$$
 + 3 ZMgBr $\xrightarrow{1.)} \Delta, 2 h$
DEE Z P Z P Z H

 $Z = Bn (1), Ph (2), 4-MeC_6H_4 (3)$

Scheme 1. Synthesis of secondary phosphine oxides by Grignard reaction.

Scheme 2. Kabachnik-Fields reaction of primary amines, paraformaldehyde and secondary phosphine oxides.

Scheme 3. Synthesis of bis(phospinoylmethyl)amines.

$$Y - NH - CH_2 - P < Bn = H (HCHO)_n + Ph P H ($$

Scheme 4. Kabachnik-Fields reaction of (aminomethyl)dibenzylphosphine oxide.

(aminomethyl)dibenzylphosphine oxides (**4b-d**) with one equivalent of paraformaldehyde and diphenylphosphine oxide (**2**) (Scheme 4). The reactions were performed in acetonitrile at 100 °C for 70 min under MW conditions, and the corresponding nonsymmetric bis(phosphine oxides) (**10b-d**) were isolated in yields of 94–97%.

Sythesis of cyclic platinum and palladium complexes

We wished to study the utilization of the bis(phosphinoylmethyl)amines (**7b-d**, **8b-d** and **9b-d**) mentioned above, therefore, the bis(dibenzylphosphinoylmethyl)amines (**7b-d**) and bis(di-*p*-tolylphosphinoylmethyl)amines (**9b-d**) were subjected to double deoxygenation applying phenylsilane. The bisphosphines obtained (**11b-d** and **12b-d**) were reacted with dichlorodibenzonitrile platinum(II) or dichlorodibenzonitrile palladium(II) (Scheme 5) to furnish cyclic transition metal complexes (**13b-d**, **14b-d**, **15b-d** and **16b-d**) in yields of 40–75%.

The catalytic activity of the platinum(II) complexes (13bd and 14b-d) was also investigated (Table 1). Because of its industrial significance, our model reaction was the hydroformylation of styrene. The catalysts formed *in situ* from bis(dibenzylphosphino) (13b-d) and bis(di(*p*-tolylphosphino) derivatives (14b-d) and tin(II)chloride were used at 100 °C. The catalytic activity of 13b-d or 14b-d was different. Applying the bis(dibenzylphosphino) derivatives (13b-d), the hydroformylation was not complete, only a moderate conversion (32–52%) was achieved (Table 1/Entry 1–3). However, in case of the bis(di(*p*-tolylphosphino) derivatives (14b-d), the conversion was almost complete after 3-8 h (Table 1/Entry 4-6). Our complexes (13b-d and 14b-d)



Scheme 5. Synthesis of cyclic platinum and palladium complexes.

Table 1. Testing our complexes in the hydroformylation of styrene.

	+ CO + H ₂	SnCl ₂ , Y-N C $100^{\circ}C$, t, 40-80 C Z = Bn (13), 4-2 $Y = {}^{n}Bu (b), {}^{c}h$	$\begin{array}{c} Z \\ CH_2 - P \\ CH_2 - P \\ DH_2 - P \\ DH_2 - P \\ DH_2 - P \\ DH_2 \\$	A B	CHO + c	
Entry	Z	Y	t [h]	Conv. [%]	R _c ^a [%]	R _{br} ^b [%]
1	Bn	^{<i>n</i>} Bu	3	32	72	65
2		۲Hex	3	50	74	61
3		Bn	3	52	70	65
4	4-MeC ₆ H ₄	"Bu	8	98	75	63
5		^c Hex	6	98	74	63
6		Bn	3	98	79	56

^aChemoselectivity towards aldehydes (A, B). [(moles of A + moles of B)/(moles of A + moles of B + moles of C) \times 100].

^bRegioselectivity towards branched aldehyde (A). [moles of A/(moles of A + moles of B) \times 100].

induced good chemoselectivity. Among the two main products, always the branched chain aldehyde (**A**) was formed in somewhat larger proportion. The Pt(II) complexes containing p-tolyl groups on the phosphorus atoms proved to be more efficient, than the complexes incorporating benzyl groups.

Conclusions

(Aminomethyl)phosphine oxides (**4b-d**, **5b-d** and **6b-d**), symmetric and nonsymmetric bis(phosphinoylmethyl)amines (**7b-d**, **8b-d**, **9b-d** and **10b-d**) were prepared by the single or double Kabachnik-Fields reactions of primary amines, paraformaldehyde and secondary phosphine oxides (**1-3**). Exploiting the advantages of the MW technique, the reactions were carried out without any catalyst.

After double deoxygenation, the bis(phosphinoylmethyl)amines (7b-d, 9b-d) were utilized as phosphine ligands in the synthesis of platinum and palladium complexes (13b-d, 14bd, 15b-d and 16b-d). The catalytic activity of the platinum complexes (13b-d and 14b-d) was tested in the hydroformylation of styrene, where the Pt(II) complexes synthesized showed high chemoselectivity and an unusual regioselectivity.

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References

- Bálint, E.; Tajti, Á.; Tripolszky, A.; Keglevich, G. Synthesis of Platinum, Palladium and Rhodium Complexes of α-Aminophosphine Ligands. *Dalton Trans.* 2018, 47, 4755–4778.
- [2] Kabachnik, M. I.; Medved, T. Y. New Synthesis of Aminophosphonic Acids. Dokl. Akad. Nauk SSSR. 1952, 83, 689–692.
- [3] Fields, E. K. The Synthesis of Esters of Substituted Amino Phosphonic Acids. J. Am. Chem. Soc. 1952, 74, 1528–1531.

- [4] Keglevich, G.; Bálint, E. The Kabachnik-Fields reaction: mechanism and synthetic use. *Molecules* 2012, 17, 12821–12835.
- [5] Bálint, E.; Tajti, Á.; Tripolszky, A. Synthesis of α-Aminophosphonates by the Kabachnik-Fields Reaction and by the Pudovik Reaction, in Keglevich G. (ed.) Organophosphorus Chemistry, Berlin: de Gruyter, 2018, pp. 118–147.
- [6] Bálint, E.; Tripolszky, A.; Jablonkai, E.; Karaghiosoff, K.; Czugler, M.; Mucsi, Z.; Kollár, L.; Pongrácz, P.; Keglevich, G.

Synthesis and Use of α -Aminophosphine Oxides and N,N-Bis(phosphinoylmethyl)amines - A Study on the Related Ring Platinum Complexes. *J. Organomet. Chem.* **2016**, *801*, 111–121.

[7] Tripolszky, A.; Keglevich, G. Synthesis of Secondary Phosphine Oxides by Substitution at Phosphorus by Grignard Reagents. *Lett. Org. Chem.* 2018, 15, 387–393.