

## A Facile Synthesis of N-Arylaminomethylphosphonates

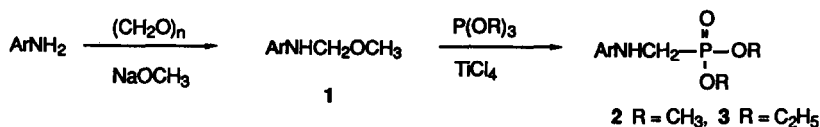
Hyun-Joon Ha\*, Gong-Sil Nam and Kyong Pae Park

Division of Chemistry  
Korea Institute of Science and Technology  
P.O.Box 131, Cheongryang, Seoul, Korea

**Summary;** *N-Arylaminomethylphosphonates were prepared from the reaction of N-(methoxymethyl)arylamines with trialkylphosphonates in the presence of titanium tetrachloride.*

Certain aminophosphonic acids as phosphorus analogues of carboxylic acids have been found to possess biological activities.<sup>1</sup> Synthesis of their esters has been developed in a wide variety of methods.<sup>2</sup> However, only two methods were reported for the preparation of N-arylaminomethylphosphonates; (1) substitution of chloromethylphosphonates with excess arylamines<sup>3</sup> (2) rearrangement of P-(halomethyl)-N-phenylphosphonamides.<sup>4</sup> Both of these are not applicable for the compounds with diverse substituents on benzene ring.

In this communication we report a new route to the synthesis of N-arylaminomethylphosphonates (2, 3) involving the condensation of N-(methoxymethyl)arylamines (1) with trialkyl phosphonates in the presence of titanium tetrachloride.<sup>5</sup> This method seems to be the simplest procedure for the synthesis in fairly good yield.



### General Procedure

N-(Methoxymethyl)arylamines (1) were prepared from arylamines, paraformaldehyde, and sodium methoxide by the reported procedure.<sup>6</sup> To a stirred solution of N-(methoxymethyl)arylamines (10 mmol) in 50 ml of methylene chloride under nitrogen was slowly added titanium tetrachloride (10 mmol) at -78 °C. After being stirred for 10 min. trialkylphosphonate (10 mmol) was added. The resulting solution was stirred at ambient temperature for 1-2 hr. After being observed that all starting material was consumed on TLC the reaction mixture was poured into water. The reaction product was extracted with methylene chloride. Organic layer was washed successively with water and brine, dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The reaction product was further purified by column chromatography or recrystallization. Results are summarized in the Table.

Table

ArNH <sub>2</sub>	ArNHCH <sub>2</sub> OCH <sub>3</sub>		R	ArNHCH <sub>2</sub> P(O)(OR) <sub>2</sub>	
	Yield <sup>a</sup> (%)	<sup>1</sup> H NMR(CDCl <sub>3</sub> ) <sup>c</sup>		Yield <sup>a,b</sup> (%)	<sup>1</sup> H NMR(CDCl <sub>3</sub> ) <sup>d</sup>
2-CH <sub>3</sub>	69	4.67(s)	CH <sub>3</sub>	70	3.61
			C <sub>2</sub> H <sub>5</sub>	87	3.50
2-OCH <sub>3</sub>	75	4.67(s)	C <sub>2</sub> H <sub>5</sub>	58	3.22
2-F	72	4.62(s)	CH <sub>3</sub>	91	3.70
			C <sub>2</sub> H <sub>5</sub>	97	3.68
4-F <sup>e</sup>	87	5.23	C <sub>2</sub> H <sub>5</sub>	92	3.67
2-F, 4-F	71	4.60(d)	C <sub>2</sub> H <sub>5</sub>	97	3.55
2-Cl, 4-Cl	89	4.70(d)	CH <sub>3</sub>	61	3.67
			C <sub>2</sub> H <sub>5</sub>	70	3.63
3-NO <sub>2</sub> , 4-Cl	97	4.80(d)	C <sub>2</sub> H <sub>5</sub>	80	3.64
2-F, 4-Br	70	4.80(d)	C <sub>2</sub> H <sub>5</sub>	74	3.67
3-CN	85	4.60(d)	C <sub>2</sub> H <sub>5</sub>	57	3.60
4-CN	82	4.70(d)	CH <sub>3</sub>	93	3.54
			C <sub>2</sub> H <sub>5</sub>	74	3.64
2-Cl,3-Cl,4-Cl	93	4.73(d)	C <sub>2</sub> H <sub>5</sub>	62	3.35

a. Yield of isolated pure product. b. Satisfactory microanalyses obtained.

c. Chemical shift of two methylene protons between nitrogen and oxygen, referenced by TMS, (s=singlet,

d=doublet). d. Chemical shift of two methylene protons between nitrogen and phosphorus, referenced by TMS,

observed as dd with coupling constants 12 and 6 Hz each. e. Perhydrotriazine was obtained as major product(ref.5)

#### References and Notes

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5. We have found that perhydrotriazines [(CH<sub>2</sub>NR)<sub>3</sub>, R = Alkyl, Aryl] were also reacted with trialkylphosphonates in the presence of titanium tetrachloride to give the same products.
6. Barluenga, J.; Bayon, A. J.; Asensio, G. *J. Chem. Soc. Chem. Commun.* 1983, 1109. Barluenga, J.; Bayon, A. M.; Campos, P.; Asensio, G.; Gonzalez-Nunez, E.; Molia, Y. *J. Chem. Soc. Perkin Trans. I* 1988, 1631

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