Heteroatom Chemistry
Volume 18, Number 1, 2007

Syntheses, Spectral Property, and Antimicrobial Activities of 6-α-Amino Dibenzo [*d,f*][1,3,2]Dioxaphosphepin 6-Oxides

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Received 15 November 2004; revised 21 April 2005

ABSTRACT: *Diethyl α-aminophosphonates (**4**) were prepared in excellent yield from three-component reaction of aldehydes (**1**), amines (**2**), and triethylphosphite (**3**) under solvent-free conditions in the presence of ceric ammonium nitrate (CAN) and were reacted with 2,2′-dihydroxybiphenyl (**5**) using p-toluene sulfonic acid monohydrate (PTSA) as a catalyst to obtain 6-α-aminodibenzo[d,f][1,3,2]dioxaphosphepin 6-oxides (**6**) in good yield. It is a first report on the cyclizations of* **4** *with* **5**. *An antimicrobial activity of numbers of* **6** *is evaluated.* © 2007 Wiley Periodicals, Inc. Heteroatom Chem 18:2–8, 2007; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20226

INTRODUCTION

Dibenzodioxaphosphocins, dioxathiaphosphocins, and dioxaphosphepins have been used as antioxidants [1,2] and superior ligands [3]. Our continuous effort to look for bioactive heterocyclic compounds led to the accomplishment of a new and efficient synthesis of 6-α-amino dibenzo[*d,f*]-[1,3,2]dioxaphosphepin 6-oxides (**6**). The procedure involves treatment of 2,2′-dihydroxybiphenyl (**5**) with various α-aminoalkyl phosphonates (**4**) in a one-pot procedure. The key intermediates of α-aminophosphonates (**4**) are known as peptidomimetics [4], antibiotics, and pharmacological agents [5,6]. Lewis acid catalyzed addition of diethyl phosphite to aldimine provided a useful method for the preparation of α-aminophosphonates [7]. Recently, three-component synthesis starting from aldehyde, amine, and diethyl/triethyl phosphite has been reported using Lewis acids such as $LiClO_4$[8] and $InCl_3$[9], and lanthanide trifolates [10] of late microwave reactions in the presence of $TaCl_5$-SiO_2[11],Al_2O_3, and montmorillonite clay [12,13] have been developed for their synthesis [14]. Due to the growing concern of the toxic influence of the organic solvent on the environment and its life forms, solvent-free organic syntheses have determined for the attention of organic chemists [15].

RESULTS AND DISCUSSION

A versatile, straightforward, and relatively inexpensive solvent-free one-pot synthesis of α-aminophosphonates (**4**) was carried out using ceric ammonium nitrate (CAN) as a catalyst. The viability of this procedure and efficiency of CAN as a catalyst was tested with several structurally varied aldehydes and amines. The reaction was successfully completed with all of them in 20–40 min affording varied yields (89–98%) depending on the nature of the reactants (Table 1). A typical experimental procedure for **4** is that a mixture of aldehyde, amine, triethylphosphite,

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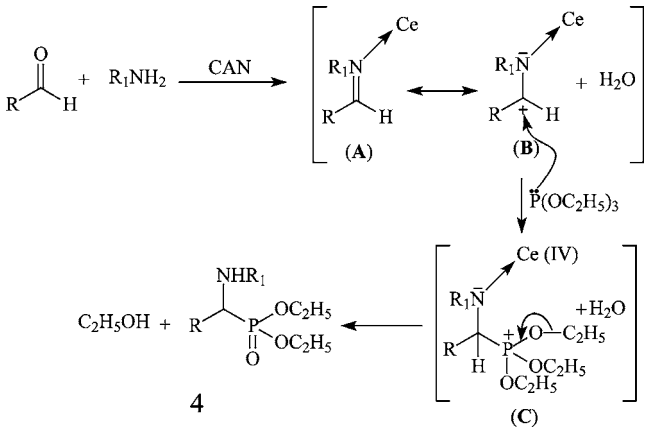
TABLE 1 Synthesis of α-Aminophosphonate (**4a–p**)

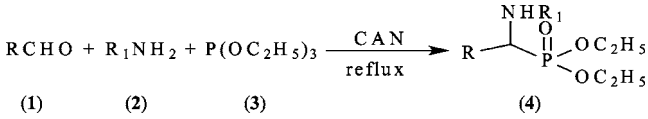
Compd.	*R*	*R_1*	*Time (min)*	*Yield (%)*	*IR (cm^{-1})*
4a	C_6H_5	C_6H_5	30	96	3331, 2982, 1604, 1512, 1240, 1025, 970, 758
4b	C_6H_5	$C_6H_5CH_2$	30	93	3328, 2973, 1617, 1514, 1226, 1014, 965, 754
4c	4—CH_3O—C_6H_5	C_6H_5	30	93	3362, 2890, 1670, 1540, 1385, 1090, 970, 730
4d	3,4—$(H_3CO)_2$—C_6H_3	2—H_3C—C_6H_4	30	96	3324, 2972, 1564, 1520, 1230, 1020, 970, 750
4e	4—HO—C_6H_4	C_6H_5	35	92	3360, 3180, 1630, 1570, 1530, 1200, 1070, 750
4f	4—H_3C—C_6H_4	2—H_3C—C_6H_4	25	96	3382, 3002, 1682, 1530, 1268, 1070, 971, 770, 562
4g	4—Cl—C_6H_4	C_6H_5	30	93	3360, 3008, 1700, 1550, 1270, 1050, 980, 770, 660
4h	4—O_2N—C_6H_4	C_6H_5	35	93	3362, 3010, 1670, 1552, 1278, 1040, 970, 776
4I	C_6H_5	CH_3O—C_6H_4	25	96	3378, 3076, 2370, 1768, 1507, 1242, 1090, 790, 730
4j	C_6H_5	2—Br, 4—H_3C—C_6H_3	30	92	3376, 3102, 2908, 1630, 1560, 1290, 1080, 962, 790, 560
4k	2—HO—C_6H_4	2—Cl—C_6H_4	40	90	3302, 3214, 3070, 1670, 1570, 1242, 1086, 980, 880, 770
4l	4—H_3C—C_6H_4	2—Br, 4—H_3C—C_6H_3	35	91	3397, 1510, 1250, 1020, 970, 780
4m	C_6H_{11}	C_6H_5	30	92	3340, 2980, 2750, 1760, 1618, 1450, 1230, 970, 840, 790, 548
4n	C_6H_5CH=CH	C_6H_5	30	90	3306, 2990, 2922, 1613, 1592, 1240, 1020, 968, 809, 702
4o	C_6H_5CH=CH	4—H_3C—C_6H_4	30	90	3306, 2970, 2910, 1610, 1590, 1240, 1010, 970, 801, 708
4p	2—Naphthyl	C_6H_5	30	93	3382, 2982, 1720, 1475, 1320, 1242, 1100, 872, 820, 762

and catalytic amount of CAN is refluxed with vigorous stirring, and the progress of the reaction was monitored by TLC. The crude α-aminophosphonates (**4**) were purified by column chromatography (see Scheme 1).

The merit of the above procedure is further proved when poor yields of α-aminophosphonate (**4a**) resulted when the same reaction is carried out with other catalyst, $Mn(OAc)_3$ with/without solvent (Table 2).

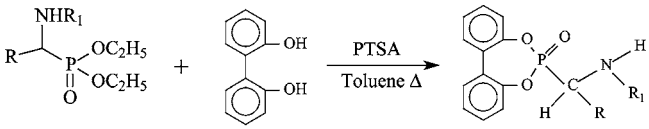
The success of this reaction may be attributed to the catalytic role played by CAN. The cerium by virtue of its strong stabilizing ability of the imine (A) and carbocation (B) facilitates initial nucleophilic attack of phosphorus at the imine carbon leading to the formation of ylide C. Further, the inherent tendency of C to break down to form more stable α-aminophosphonates (**4**) drives the reaction to completion.





SCHEME 1

The reaction of *O, O*-diethyl α-aminophosphonates (**4**) with 2,2-dihydroxybiphenyl (**5**) in the presence of *p*-toluene sulfonic acid (PTSA) as a catalyst in toluene with stirring at reflux temperature afforded 6-α-aminodibenzo[*d,f*][1,3,2]dioxaphosphepin 6-oxides in high yield (Table 3). Ethanol formed during the course of the reaction was distilled out along with toluene till its volume was reduced to half to prevent a reverse reaction. It is a first report on similar cyclizations using PTSA.



4 5 6

Compd.	R	R_1
6a	C_6H_5	C_6H_5
6b	C_6H_5	$C_6H_5CH_2$
6c	4-CH_3O-C_6H_4	C_6H_5
6d	4-H_3C-C_6H_4	2-CH_3-C_6H_4
6e	C_6H_5	4-CH_3-C_6H_4
6f	C_6H_5	2-Br-4-H_3C-C_6H_3
6g	C_6H_5CH=CH	C_6H_5
6h	4-H_3C-C_6H_4	2-Br-4-H_3C-C_6H_3

All the members of **6** exhibited characteristic IR absorption [16,17] for P=O and P—$OC_{(aromatic)}$ groups. In their ^1H NMR spectra, phenylaminobenzyl dibenzodioxaphosphepin moieties showed complex multiplets in the range of 6.60–7.7 for the 18 protons.

TABLE 2 Effect of the Solvent and Reagents

Compd.	*Solvent*	*Reagent*	*Yield (%)*
4a	CH_3CN	$Mn(OAc)_3$	78
4a	No solvent	$Mn(OAc)_3$	80
4a	CH_3CN	CAN	82
4a	No solvent	CAN	96

P-CH methylene proton in all the compounds appeared as a doublets in the range of 4.42–5.0 ($^2J_{CH—P}$ = 22.5–24.36 Hz). The aliphatic methyl and methoxy protons of 6-substituted moieties exhibited signals at δ 2.10 and 3.95, respectively. Then ^{13}C NMR chemical shifts (see Tables 4 and 5) were interpreted based on comparison with carbon chemical shifts of **5** and related systems [17,18]. The ^{31}P NMR signals are observed in the range of 29.2–43.9 ppm [19] for 6-substituted-α-aminodibenzo [*d,f*][1,3,2]dioxaphosphepin 6-oxides (**6 a–h**) (see Table 3).

ANTIMICROBIAL ACTIVITY

Antibacterial activity [20] of **6a–h** was screened against the growth of *Staphylococcous aureus* (gram positive) and *Klebsiella pneumoniae* (gram negative) at concentrations 200 and 400 ppm. All these compounds exhibited high activity against both the organisms. Similarly, their antifungal activity was also studied against the growth of *Pellicularia solmanicolor* (pink disease) and *Macrophomina phoseolina* (dry root rot of sunflower and citrus) at two different concentrations (200 and 400 ppm) [21]. All these results are presented in Table 6. Most of the compounds showed good antifungal activity against the growth of both the fungi. Penicillin and griseofulvin was used as a reference standard for bacteria and fungi, respectively.

It is interesting to note that the compounds **6c–h** exhibited very high antimicrobial activity. Compounds **6c–h** exhibited very high activity against *Klebsiella pneumoniae* when compared to the activity of the standard penicillin. The compound **6d** showed the highest activity. In view of their very strong antibacterial activity, further detailed study on the evaluation of their antimicrobial activity is in progress to explore their commercial applications.

EXPERIMENTAL

All reactions were carried out under anhydrous conditions in nitrogen atmosphere. Melting points were determined in Mel-Temp apparatus using open capillary tubes and are uncorrected. IR spectra (ν_{max}, cm^{-1}) were measured with Shimadzu-435/Perkin Elmer 1000 FTIR. NMR spectra were taken on a Bruker AC 300 spectrometer operating at 300 MHz for ^1H, 75.45 MHz for ^{13}C, and 121.7 MHz for ^{31}P NMR. Chemical shifts of ^1H and ^{13}C were expressed in δ (ppm) downfield from an internal standard tetramethylsilane (TMS). ^{31}P chemical shifts are expressed in δ (ppm) with respect to 85% phosphoric acid used as external standard. Microanalyses were performed at the Central Drug Research Institute (CDRI) Lucknow, India. TLC monitoring was carried out using precoated Kieselgel $60F_{254}$ plates (E-Merck).

O,O-Diethyl 6-α-aminophosphonates **4a–p**

General Procedure: A mixture of the aldehyde (**1**, 5 mmol), amine (**2**, 5 mmol), and triethylphosphite (**3**, 5 mmol) and catalytic amount of ceric ammonium nitrate (CAN) was stirred under reflux for 30 min. After completion of the reaction as indicated by TLC, the residue was purified by column chromatography (60–120 mesh silicagel) using ethyl acetate-hexane (1:2) as an eluent to afford pure α-aminophosphonates as solids. Synthetic and spectral data for **4a–p** are given in Tables 1, 3, and 4.

TABLE 3 Synthesis of 6-α-Aminodibenzo[*d,f*][1,3,2]dioxaphosphepin 6-oxides (**6a-h**)

				Elemental Analysis (%)					
				Calcd.		*Found*			
Compd.	*mp (°C)*	*Yield (%)*	*M. Formula (Molec. weight)*	*C*	*H*	*C*	*H*	*^{31}P NMR (ppm)*	*IR (cm^{-1})*
6a	148–150	82	$C_{25}H_{20}NO_3P$ (413.275)	72.63	4.86	72.50	4.70	37.8	3340, 1302, 1195, 965
6b	172–173	75	$C_{26}H_{22}NO_3P$ (427.30)	73.06	5.11	72.87	5.00	43.4, 43.9	3310, 1308, 1221, 985
6c	140–141	80	$C_{26}H_{22}NO_4P$ (443.32)	70.42	5.06	70.28	4.92	31.8	3320, 1299, 1235, 969
6d	168–169	76	$C_{27}H_{24}NO_3P$ (441.30)	73.46	5.47	73.30	5.33	38.2, 38.8	3325, 1299, 1189, 968
6e	152–153	72	$C_{26}H_{22}NO_4P$ (443.32)	70.42	5.06	70.26	4.92	41.2, 41.9	3335, 1298, 1206, 957
6f	139–140	70	$C_{26}H_{21}BrNO_3P$ (506.28)	61.67	4.18	61.51	4.08	29.2, 30.1	3308, 1295, 1223, 961
6g	165–166	74	$C_{27}H_{22}NO_3P$ (439.30)	73.79	5.04	73.60	5.00	39.8	3327, 1308, 1202, 952
6h	178–180	72	$C_{27}H_{23}BrNO_3P$ (520.32)	62.32	4.45	62.16	4.31	31.2, 31.7	3315, 1290, 1208, 945

TABLE 4 ^{1}H and ^{13}C NMR Data of **4a–p**

Compd.	*^{1}H NMR* δ	*^{13}C NMR*
4a	1.1 (t, 3H, $J = 7.1$ Hz),1.28 (t, 3H, $J = 7.1$ Hz), 3.68–4.15 (m 4H), 4.75 (d, 1H, $J = 24.1$ Hz), 6.72 (t, 1H, $J = 7.3$ Hz) 7.12 (t, 2H, $J = 7.3$ Hz), 7.23 (m, 1H), 7.34 (t, 2H, $J = 7.2$Hz), 7.5 (m, 2H).	16.2, 16.5, 59.5, 62.8, 63.0, 127.2, 128.0, 128.4, 128.6, 128.75, 1289.9, 135.5, 139.6
4b	1.18 (t, 3H, $J = 7.2$ Hz), 1.30 (t, 3H, $J = 7.1$ Hz), 2.2 (s, 3H), 3.72–3.82 (m, 1H), 3.95–4.2 (m, 3H), 4.71 (dd, 1H, $J = 23.8$, 7.0 Hz), 5.3 (dd, 1H, $J = 7.0$, 2.0 Hz), 6.30 (d, 1H, $J = 7.8$ Hz), 6.78 (d, 1H, $J = 7.8$ Hz), 7.26–7.52 (m, 6H)	16.4, 16.6, 56.3, 63.5, 113.0, 118.5, 128.0, 128.7, 129.2, 130.0, 136.0, 146.3
4c	1.17 (t, 3H, $J = 7.1$ Hz), 1.23 (t, 3H, $J = 7.1$ Hz), 3.67 (s, 3H), 3.94–4.17 (m, 4H), 4.82 (d, 1H, $J = 23.6$ Hz), 6.61–6.72 (m, 5H), 6.80–6.96 (m, 2H), 7.10–7.22 (m, 2H)	16.4, 16.5, 55.3, 55.6, 63.4, 114.1, 118.2, 120.4, 125.2, 127.8, 129.0, 132.7, 146.5, 150.4
4d	1.14 (t, 3H, $J = 6.6$ Hz), 1.20 (t, 3H, $J = 6.7$ Hz), 2.31 (s, 3H), 3.64–3.70 (m, 4H), 3.82 (s, 6H), 3.92–4.18 (m, 3H), 4.72 (d, 1H, $J = 23.8$ Hz), 6.42 (d, 1H, $J = 7.8$ Hz), 6.64 (d, 1H, $J = 7.6$ Hz), 6.80 (d, 1H, $J = 7.4$ Hz), 6.94–7.10 (m, 9H)	16.2, 16.4, 20.2, 54.6, 55.6, 57.4, 62.8, 62.9, 110.8, 110.9, 111.0, 113.8, 119.8, 120.0, 127.2, 128.2, 129.4, 144.0, 144.8, 148.4, 148.6, 148.9
4e	1.18 (t, 3H, $J = 6.8$ Hz), 1.26 (t, 3H, $J = 6.7$ Hz), 3.9–4.18 (m, 4H), 4.95 (d, 1H, $J = 23.8$ Hz), 6.62–6.8 (m, 3H), 6.80–6.96 (m, 2H), 7.12–7.30 (m, 4H), 8.86 (br, s, 1H, OH)	16.4, 16.6, 47.8, 50.6, 62.2, 63.6, 114.0, 115.8, 118.5, 120.0, 129.2, 130.0, 131.8, 132.2, 151.7, 158.4, 159.6
4f	1.18 (t, 3H, $J = 7.0$ Hz), 1.26 (t, 3H, $J = 7.0$ Hz), 2.25 (s, 3H), 2.31 (s, 3H), 3.60–3.82 (m, 1H), 4.05–4.16 (m, 2H), 4.62 (br, s, 1H, NH),4.72 (d, 1H, $J = 23.6$ Hz), 6.36 (d, 1H, $J = 8.0$ Hz), 6.62 (t, 1H, $J = 8.0$ Hz), 7.0 (t, 1H, $J = 8.1$ Hz), 7.10 (d, 2H, $J = 8.2$ Hz) 7.36 (d, 2H, $J = 8.2$ Hz)	16.1, 16.2, 16.3, 17.3, 20.6, 54.2, 57.2, 62.8, 63.0, 111.2, 117.8, 122.6, 126.7, 127.4, 127.6, 129.0, 129.2, 129.8, 132.6, 132.7, 137.4, 137.6, 144.0, 144.5
4g	1.16 (t, 3H, $J = 6.8$ Hz), 1.28 (t, 3H, $J = 6.8$ Hz), 3.62–3.82 (m, 2H), 4.07–4.2 (m, 2H), 4.63 (br, s, 1H); 6.6 (t, 1H, $J = 7.4$ Hz), 6.62–6.89 (m, 5H), 6.9–7.10 (m, 2H), 7.11–7.30 (m, 2H)	16.2, 16.4, 59.5, 62.8, 63.2, 127.2, 128.2, 128.6, 128.8, 128.9, 130.0, 135.8, 146.5
4h	1.18 (t, 3H, $J = 7.0$ Hz), 1.30 (t, 3H, $J = 7.0$ Hz), 3.7–3.87 (m, 2H), 4.17–4.3 (m, 2H), 4.70 (br, s, 1H), 6.58 (t, 1H, $J = 7.4$ Hz), 6.7–7.1 (m 5H), 7.32–7.48 (m, 2H), 8.0–8.08 (m, 2H)	16.3, 16.5, 59.5, 62.8, 63.8, 127.2, 128.4, 128.6, 129.2, 129.6, 130.0, 135.8, 146.4, 150.8
4i	1.15 (t, 3H, $J = 6.8$ Hz), 1.26, (t, 3H, $J = 6.8$ Hz), 3.67 (s, 2H), 3.61–4.19 (m, 4H), 4.66 (d, 1H, $J = 24.0$ Hz), 6.52 (d, 2H, $J = 8.2$ Hz) 6.68 (d, 2H, $J = 8.2$ Hz), 7.21–7.38 (m, 3H), 7.40–7.50 (m, 2H)	15.7, 15.8, 15.9, 16.2, 20.6, 54.2, 58.0, 62.4, 62.8, 70, 113.4 114.6, 114.8, 121.9, 127.1, 127.4, 127.8, 127.9, 120.0 128.1, 128.3, 129.4, 132.2, 135.6, 139.8, 140.2, 152.0
4j	1.15 (m, 3H, $J = 7.2$ Hz), 1.28 (m, 3H, $J = 7.0$ Hz), 2.25 (br, s, 1H, NH), 3.50 (d, 1H, $J = 11.8$ Hz), 3.72–4.16 (m, 6H), 7.22–7.46 (m, 6H), 7.22–7.50 (m, 1H)	16.2, 16.3, 16.5, 19.7, 56.0, 57.0, 63.2, 63.3, 110.4, 112.6, 127.6, 127.8, 127.9, 128.3, 128.5, 128.7, 132.6, 135.4, 135.6, 140.8, 141.0

(Continued)

TABLE 4 Continued

Compd.	^{1}H *NMR* δ	^{13}C *NMR*
4k	1.18 (t, 3H, $J = 7.2$ Hz), 1.24 (t, 3H, $J = 7.2$ Hz), 3.80–3.92 (m, 1H), 4.05–4.20 (m, 3H), 4.80 (br, s, 1H, NH), 5.05 (d, 1H, $J = 23.9$ Hz), 6.57 (d, 2H, $J = 7.8$ Hz), 6.82 (t, 1H, $J = 7.6$ Hz), 6.84 (d, 1H, $J = 7.6$ Hz), 9.05 (br, s, 1H, 6H)	16.4, 16.5, 46.8, 50.3, 62.6, 63.4, 115.6, 118.4, 120.8, 129.4, 130.9, 132.0 132.4, 150.6, 158.9, 159.6
4l	1.18 (t, 3H, $J = 7.0$ Hz), 1.29 (t, 3H, $J = 7.0$ Hz), 2.18 (s, 3H), 2.38 (s, 3H), 3.8–3.86 (m, 1H), 3.9–4.20, (m, 3H), 4.70 (d, 1H, $J = 7.8$ Hz), 6.80 (d, 1H, $J = 7.6$ Hz), 7.10 (d, 2H, $J = 7.8$ Hz), 7.20–7.40 (m, 3H)	16.4, 16.6, 20.3, 21.4, 59.4, 62.6, 62.8, 64.0, 114.8, 118.6, 129.6, 129.8, 130.0, 130.6, 135.2, 136.4, 146.8, 147.9
4m	1.12 (t, 3H, $J = 7.2$ Hz), 1.28 (t, 3H, $J = 7.2$ Hz), 1.30–1.86 (m, 1H), 2.63 (dd, 1H, $J = 19.0$, 20.0 Hz), 3.95–4.15 (m, 4H), 6.65–7.15 (m, 5H)	16.4, 22.0, 27.2, 28.4, 29.8, 31.2, 39.9, 56.1, 62.6, 113.4, 117.8, 129.7, 129.9, 147.8
4n	1.17 (t, 1H, $J = 7.0$ Hz), 1.23–1.38 (m 3H), 3.18 (br, s, 1H, NH), 4.15–4.22 (m, 4H), 4.45 (dd, 1H, $J = 2.2$, 2.1 Hz), 6.18–6.35 (m, 1H), 6.58–6.67 (m, 3H), 6.88–7.20 (m, 2H), 7.20–7.40 (m, 4H)	16.3, 20.2, 55.7, 62.7, 62.8, 63.4, 113.4, 123.6, 126.4, 127.6, 128.4, 129.6, 132.7, 133.0, 136. 2, 143.8
4o	1.23–1.38, (m, 6H), 2.25 (s, 3H), 3.18 (br, s, 1H, NH), 4.15–4.22 (m, 4H), 4.45 (dd, 1H, $J = 2.2$, 2.1 Hz), 6.18–6.35 (m, 1H), 6.58–6.67 (m, 3H), 6.7–6.92 (m, 2H), 7.22–7.39 (m, 4H)	16.3, 20.1, 52.8, 55.9, 62.2, 62.7, 63.1, 113.6, 123.6, 126.2, 127.4, 128.4, 129.2, 132.8, 132.9, 136.2, 144.0
4p	1.10 (t, 3H, $J = 7.0$ Hz), 1.30 (t, 3H, $J = 7.0$ Hz), 1.80 (br, s, 1H, NH), 3.60 (m, 1H), 3.9 (m, 1H), 4.15 (m, 2H), 4.76 (d, 1H, $J = 23.8$ Hz), 6.56–6.72 (m, 3H), 7.02–7.15 (m, 2H), 7.38–7.55 (m, 2H), 7.60 (d, 1H, $J = 7.76$ Hz), 7.75–7.82 (m, 4H)	15.6,15.8, 16.4, 16.5, 50.2, 53.2, 63.4, 113.6, 118.4, 122.9, 125.4, 125.8, 125.9, 126.2, 128.4, 128.6, 128.9, 129.2, 132.0 132.4, 133.4, 145.9, 146.2

TABLE 5 ^{1}H and ^{13}C NMR Data of **6a–h**

Compd.	^{1}H *NMR*	^{13}C *NMR*
6a	5.0 (d, 1H, $J = 24.4$ Hz), 6.47 (d, 1H) 6.94–7.5 (m, 18H)	53.7 ($J = 110$ Hz) 114.0, 117.2, 118.9, 121.0, 126.5, 128.1, 128.5 , 129.3, 130.0, 131.0, 134.0, 145.5, 153.2
6b	4.1 (d, 1H, $J = 24.4$ Hz), 4.7 (m, 1H), 6.30 (br, s, 1H, NH), 6.8–7.54 (m 18H)	56.3 ($J =$ 121. Hz), 114.0, 118.5, 128.6, 128.9, 129.4, 130.0, 136.4, 146.8
6c	3.64 (s, 3H), 4.80 (d, 1H, $J = 23.8$ Hz), 6.65 (brs, 1H, NH) 6.8–7.42 (m, –18H)	55.4 ($J = 128$ Hz) , 55.6, 114.2, 118.2, 120.3, 125.2, 127.7, 129.0, 132.6, 146.8, 150.9,
6d	2.28 (s, 3H), 2.35 (s, 3H), 4.6 (br, s, 1H, NH), 5.2 (d, 1H, $J = 23.4$ Hz), 6.60–7.46 (m,–16 H)	16.4, 17.2, 20.8, 57.1 ($J = 120$ Hz), 63.0, 117.7, 122.6, 126.6, 127.3, 127.4, 132.6, 137.1, 137.3 145.0, 146.0.
6e	3.60 (s, 3H), 4.66 (d, $J =$ 22.8 1H), 6.10 (br, s, 1H, NH), 6.68–7.6 (m, 17H)	55.4, 56.31 ($J = 126$ Hz), 114.3, 114.8, 121.4, 127.2, 127.4, 127.6, 127.5, 128.6, 132.5, 135.0, 139.8, 142.1, 152.2
6f	2.37 (s, 3H,) 4.29 (m, 1H), 6.0 (br, s, 1H, NH) 6.8–7.4 (m, 18 H)	19.0, 56.2 ($J = 130$ Hz), 120.0, 125.0, 128.0, 128.4, 128.4, 130.0, 130.4, 131.2, 136.0, 136.2, 143.0, 154.0.
6g	4.22 (m, 1H), 6.13–6.35 (m, 1H), 6.65–7.7 (m, 18H)	55.6 ($J = 113.2$ Hz), 113.0, 123.5 126.3, 127.5, 128.3, 129.5, 132.6, 136.8, 140.0, 142.8, 150.0, 154.8
6h	2.18 (s, 3H), 2.26 (s, 3H), 4.42 (m, 1H), 6.8–7.43 (m, 15H)	20.3, 21.2, 57.2 ($J = 115$ Hz) , 114.8, 118.6, 120.8, 129.0, 131.6, 136.0, 142.0.

TABLE 6 Antibacterial and Antifungal Activity of **6a–h**

	Zone of inhibition (%)							
	Fungi				*Bacteria*			
	P. solmanicolor		*M. phaseolina*		*S. aureus*		*K. pneumonaie*	
Compd.	200[a]	400[a]	200[a]	400[a]	200[a]	400[a]	200[a]	400[a]
6a	9	30	10	24	8	33	18	32
6b	20	38	18	31	23	48	30	53
6c	30	51	18	31	23	48	30	53
6d	26	50	26	40	40	60	42	61
6e	29	49	22	42	33	49	20	38
6f	30	56	26	50	40	66	27	50
6g	34	59	20	48	24	54	28	54
6h	40	62	23	50	30	50	28	60
Griseofulvin	20		21		–		–	
Penicillin	–		–		22		24	

[a]Concentration in ppm.

6-α-aminodibenzo[d,f][1,3,2] dioxaphosphepin 6-oxides **6a–h**

General Procedure: A mixture of α-aminophosphonate (**4**, 2 mmol) and 2,2-dihydroxy-biphenyl (**5**, 2 mmol) and catalytic amount of *p*-toluene sulfonic acid in toluene (50 mL) was kept stirred under reflux. 50% of toluene was distilled off during the course of reaction to remove ethanol formed in the reaction. After completion of the reaction as indicated by TLC analysis, the reaction mixture was cooled to room temperature and quenched by addition of saturated. $NaHCO_3$ solution. The reaction mixture was extracted with ethyl acetate, and the combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness to obtain 6-α-aminodibenzo [*d, f*][1,3,2]dioxaphosphepin 6-oxides (**6a–g**) as solids. Synthetic and spectral data for **6a–h** are given in Tables 1, 3, 4 and 5.

CONCLUSIONS

In summary, we have developed a new and efficient method for the preparation of α-aminoalkyl phosphonates from an aldehyde, amine and triethylphosphite in the presence of catalytic amount CAN. Also an expeditious method for the synthesis of 6-α-aminodibenzo[*d, f*][1,3,2] dioxaphosphepin 6-oxides is accomplished by the cyclization reaction of α-aminoalkylphosphonate with 2,2-dihydroxyphenyl in the presence of PTSA. This is the first successful report on similar cyclizations.

ACKNOWLEDGMENTS

We thank Dr. C. Nagaraju, Department of Chemistry, Sri Venkateswara University, Tirupati, India for helpful discussions and to Dr. G. M. Sundaravalli, Department of English, Sri Venkateswara University, Tirupati, India for correcting in English the manuscript and the Director, Central Drug Research Institute (CDRI), Lucknow, Shasun Chemical and Drug Ltd., Chennai, India for analytical data, MK is grateful to CSIR, New Delhi, India for the award of Senior Research Fellowship.

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