This document is the accepted manuscript version of the following article:
N. M. Neisius, M. Lutz, D. Rentsch, P. Hemberger, S. Gaan (2014). Synthesis of DOPO
based Phosphonamidates and their Thermal Properties, Industrial & Engineering Chemistry
Research 53, 2889-2896. <http://doi.org/10.1021/ie403677k>

Synthesis of DOPO based Phosphonamidates and their Thermal Properties

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KEYWORDS DOPO, phosphonamidate, flame retardants, thermal stability, chlorination, Atherton Todd Reaction, synthesis, organophosphorus.

ABSTRACT

Synthetic strategies for the preparation of 9,10 dihydro 9,10 oxa 10 phosphaphenanthrene 10 oxide (DOPO) derivatives are of special interest for polymer industry as well as academia involved in development of halogen free flame retardant additives. In this work various amino DOPO derivatives (phosphonamidates) were synthesized by employing three different synthetic methods involving various chlorinating agents. The synthetic methods were compared with regards to purity and yield of the resulting amino DOPO derivatives. The chlorinating agents that were used in this work are namely CCl_4 , trichloroisocyanuric acid (TCCA) and sulfuryl chloride. Some compounds e.g. amine substituted DOPO derivative could be synthesized using sulfuryl chloride with a yield >94% and a purity >99%. As proof of possible future industrial scale up up scaling laboratory trials in 500 g scale were also performed for two methods. The synthesized compounds were characterized for their melting point and thermal stability by using thermogravimetric analysis (TGA) and direct probe insertion mass spectrometry (DIP/MS). In general these amino DOPO derivatives exhibited high thermal stability with some having stability >320 °C.

1. Introduction

Organophosphorus compounds are ubiquitous and valuable building blocks and additives for application in miscellaneous fields in chemical industry as well as academia.¹ In academic research they are used in organic synthesis in coordination chemistry, catalysis and biochemistry and they are also commonly used in several commercial applications such as pesticides, electrolytes or additives in polymers as lubricants or antioxidants.² Since more and more halogenated flame retardants have been suspected to cause health problems³ and to be

ecologically harmful⁴ and bio accumulative⁵, the development of new organophosphorus compounds as their replacement is becoming popular and there is an immense interest of researchers as well as industry in their novel derivatives. Organophosphorus compounds can be either applied as finishing additive⁶ or added to the polymer during its polymerization process or it's further processing.⁷ A variety of polymers, such as polyester or polyamide are processed by melt extrusion at elevated temperatures of >250 °C. Therefore flame retardant additives for such kind of polymers need to be thermally stable and unreactive at elevated processing temperatures for considerable duration of time. Furthermore it is also desirable that the melting points of such additives should also be in a similar temperature range so as to ensure good dispersion and avoid rheological problems. Among the various classes of organophosphorus flame retardant compounds, 9,10 dihydro 9,10 oxa 10 phosphaphenanthrene 10 oxide (DOPO) and its derivatives have attracted a lot of attention recently due to its gas phase flame inhibition mechanism.^{2e, 8} It is proposed that this gas phase flame inhibition mechanism is similar to that of halogenated flame retardants.

A phosphorus based flame retardant releases small low energy radicals, such as PO*, in the gas phase during its decomposition.⁹ These low energy radicals can react with high energy radicals such as hydroxyl or hydrogen radicals from the decomposing polymer as shown in equation (1) and (2).

A subsequent reaction of HPO with H* and OH* radicals leads to a regeneration of the active PO* species. Thus the flame retardant action of PO*, that leads to a lower release of energy/heat

and subsequently a cooling down and extinguishing of the flame, can be considered as catalytic effect (equation (3) and (4)).

In addition to its good gas phase flame inhibition effect, preliminary toxicological and ecological studies reveal that DOPO exhibits very low toxicity which was determined by toxicity tests towards the water flea *Daphnia magna* according to OECD guidelines 202.¹⁰ Thus DOPO and its derivatives are considered as efficient and eco friendly alternative or replacement for toxic halogenated flame retardant additives.

In our earlier studies we have reported that P N bonded organophosphorus molecules such as phosphoramidate compounds show a remarkably higher flame retardant efficiency in flexible polyurethane foam matrices as compared to P O bonded phosphate analogues¹¹. In continuation to this preliminary work, we have further designed novel P N bonded structures based on DOPO.^{8b} The conversion of the P H bond of DOPO to a P N bond leads to the desired phosphonamidate derivatives. In literature one can find syntheses of such phosphonamidate molecules from DOPO via two common synthetic ways.

The first way involves a simple one step Atherton Todd reaction (ATR) using CCl_4 as chlorinating agent (Scheme 1).¹²

It is reported for a few examples in literature that this reaction results in the formation of DOPO based phosphonamidates in good to excellent yields up to 87% without any additional difficult or time consuming purification steps.^{8c f} The major drawback of this method is the use of CCl_4 , which is relatively expensive and more importantly, it is carcinogenic and harmful to the

environment. Its use as solvent and reagent in industrial chemical production is especially not attractive in Europe. Thus a suitable replacement for CCl_4 as chlorination agent for the conversion of a P H bond to an intermediate P Cl bond is desirable. The second common way of synthesizing such phosphoramidates is via a two step reaction sequence starting from trivalent DOP Cl **2** with subsequent H_2O_2 oxidation(Scheme 2).¹³

Although this method avoids the use of CCl_4 it creates other synthetic challenges such as hydrolysis or trans esterification reactions when using H_2O_2 as an oxidizing agent.¹⁴ Furthermore the chemical functional group tolerance is limited due to the use of a strong oxidizing agent and a multi step synthetic procedure is usually complex and results are not always reproducible.

In this work we have evaluated two different alternative synthetic methods other than ATR for the preparation of DOPO based phosphoramidates. We have screened two alternative chlorinating agents and compared the synthesis results (the yield and the purity of the resulting compounds) with the CCl_4 method, (Scheme 3).

The two alternative chlorinating agents used in this work are namely trichloroisocyanuric acid (TCCA) and sulfuryl chloride. Trichloroisocyanuric acid is a cheap and relatively environmentally friendly chlorinating agent. Cyanuric acid, which is the by product formed during the chlorination of P H bond, can be easily isolated and recycled by re chlorination. Furthermore it is also atom economic because only $1/3^{\text{rd}}$ equivalent is needed for chlorination for one equivalent of P H moiety. From a sustainable point of view, TCCA would be a very desirable chlorinating agent. The use of TCCA as an efficient and fast chlorinating agent for phosphites has been described earlier in the literature.¹⁵ Its application on phosphinites or more

specifically on DOPO has not been reported or investigated so far. Scientific reports on using sulfuryl chloride as chlorinating agent for phosphites are also rare.¹⁶ Furthermore there is no report of such reactions in scales bigger than few millimoles. The advantage of using sulfuryl chloride as chlorinating agent would be that the only by products SO₂ and HCl formed during the reaction, are gaseous and can thus be removed easily from the reaction mixture and trapped as salts in alkaline media. For both chlorinating agents, the intermediate DOPO Cl **3**, can either be isolated or reacted *in-situ* with an appropriate amine to obtain the desired phosphonamidate compound. In this work we have followed the *in-situ* route without any isolation of DOPO Cl **3** and further reaction with seven different amines. The choice of amines was driven by the idea to show that a certain number of chemical functionalities, such as additional ester, ether or amino groups and C C double bonds are compatible with the reaction conditions. Furthermore we wanted to show that it is possible to create DOPO derivatives that exhibit a wide range of thermal stabilities, melting point and gas phase availability which is important for the application as flame retardant additive in different polymeric. Up scaling laboratory trials in 500 g scale further proves the suitability of such synthetic methods for industrial production of DOPO derivatives.

2. Experimental Section

2.1 Materials Benzylamine, ethylenediamine, allylamine, n propylamine, 2 methoxyethylamine, glycinemethylester hydrochloride, piperazine, triethylamine, methylene chloride, carbon tetrachloride, acetonitrile, sulfuryl chloride and trichloroisocyanuric acid were purchased from Sigma Aldrich, Switzerland. All reagents and chemicals were used without

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3 further purification. DOPO was provided by Krems Chemie Chemical Services AG (KCCS) with
4 a purity >97% and was used as received.
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7 8 **2.2 Characterization** 9

10 All compounds were analyzed by gas chromatography/mass spectroscopy (GC/MS) and ^1H , ^{13}C ,
11 and ^{31}P NMR to ensure the purity and confirm their structure. For GC/MS analyses, a gas
12 chromatograph coupled with mass spectrometer was used (Agilent GC6890/MS 5973). Helium
13 was used as the carrier gas. Aliquots (1 μL) from the crimp sealed vials were injected by use of
14 an automated sampler. The split/splitless injection inlet was maintained at 250 $^{\circ}\text{C}$, and samples
15 were separated on a 30 m capillary column coated with a 0.25 μm film of (5%
16 phenyl)methylpolysiloxane. A 10:1 split ratio was used. The temperature program consisted of
17 an isothermal separation at 280 $^{\circ}\text{C}$ for 30 min. The NMR analyses were performed on a Bruker
18 NMR machine. The ^1H NMR analyses were measured with a frequency of 400 MHz, while the
19 ^{31}P NMR and ^{13}C NMR measurements were run at a frequency of 162 MHz and 100 MHz
20 respectively. Infrared spectra were recorded on a Bio Rad FTS 175 IR spectrometer.
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36 The thermal stability of the DOPO derivatives was studied using a NETZSCH TG 209 F1
37 instrument and a 2.5 mg sample in a nitrogen environment (50 mL/min) at a heating rate of
38 10K/min from 50 to 800 $^{\circ}\text{C}$. Three measurements were conducted for each sample system to
39 ensure the reproducibility of the results. The presented curves are averages curve of three
40 measurements.
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47 Direct insertion probe mass spectrometry (DIP MS): DIP MS was used to evaluate the gas phase
48 availability and the degradation processes of these DOPO derivatives. The sample was
49 introduced into a quartz micro cup in contact with a heating probe, the tip of which was inserted
50 into the ionization chamber maintained at strongly reduced pressure. In this study, DIP MS
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analyses were conducted for a 1-2 μgm sample of FPUF using a ThermoQuest FINNIGAN apparatus. The probe was heated from 50 $^{\circ}\text{C}$ to 450 $^{\circ}\text{C}$ at a rate of 50 K/min. The final temperature was maintained for one more minute. The pressure was 10^{-6} mbar.

2.3 Experimental procedures for small-scale (5g) reactions

Small-scale reactions using the CCl_4 method (A) were run under similar conditions as already described in literature.¹⁵⁻¹⁶ Small-scale reaction conditions for method B and C are based on reported methods but were finally performed with major modifications. Detailed reaction procedures can be found in the supporting information.

2.4 Experimental procedures for synthesis of EDA-DOPO (10) in 500g scale

CCl_4 Method: 9,10 dihydro 9 oxa 10 phosphaphenanthrene 10 oxide (DOPO) **1** (500 g, 2.31 mol), triethylamine (353 mL, 2.54 mol) and ethylene diamine (73.5 mL, 1.1 mol) are dissolved in 2L of dichloromethane, stirred and cooled to 0 $^{\circ}\text{C}$. After the solution has been cooled down, carbon tetrachloride (246 mL, 2.54 mol) is added dropwise at a rate that the reaction temperature does not exceed 15 $^{\circ}\text{C}$. After all CCl_4 has been added, the solution is allowed to warm up to room temperature and stirring is continued overnight. The desired product precipitates from the solution together with triethylamine hydrochloride as a white solid. Subsequently the reaction mixture is filtered and all solid material is collected. The precipitate is washed with water (3x 1L) to remove triethylamine hydrochloride from the mixture. The resulting white solid is washed twice with acetone (500 mL each) and then dried in vacuum at 50 $^{\circ}\text{C}$ until no more water and acetone is left. Finally the pure product **10** is isolated as a 1:1 mixture of diastereomers with a yield of 85% (457 g, 0.93 mol).

SO_2Cl_2 method: A 3L three neck flask equipped with reflux condenser, dropping funnel and gas washing bottle (filled with sodium hydroxide solution) is filled with a solution of 500 g (2.31

mol) of 9,10 dihydro 9 oxa 10 phosphaphenanthrene 10 oxide (DOPO) **1** in 1.5 L CH₂Cl₂ under a nitrogen atmosphere. The mixture is kept at room temperature with an external water bath cooling while sulfuryl chloride (187.5 mL, 2.32 mol) is added dropwise. An immediate gas evolution of HCl and SO₂ can be observed. After complete addition (~3h) the reaction mixture is heated to reflux until no more gas evolution can be observed (about 3 4h). Afterwards the reaction mixture is cooled to room temperature and a solution of ethylene diamine (73.5 mL, 1.1 mol) together with triethylamine (353 mL, 2.54 mol) in 500 mL CH₂Cl₂ is added dropwise at a rate that the reaction temperature of the reaction mixture does not exceed 30 °C. Subsequently the reaction mixture is stirred over night at room temperature. The white precipitate that contains triethylamine hydrochloride as well as EDA DOPO **10** is separated by filtration. The filtercake is washed several times with deionized water (3x 1L) to remove triethylamine hydrochloride and two times with 500 ml of acetone. The resulting solid is dried in vacuum to give 445 g (0.91 mol, 83%) EDA DOPO **10** as a 1:1 mixture of diastereomers in sufficient purity.

Analytical data for EDA DOPO **10**:

m.p. 272 °C

¹H-NMR (DMSO-d₆) δ (ppm): 8.13-8.22 (m, 4H), 7.72-7.86 (m, 4H), 7.56 (m_c, 2H), 7.40-7.49 (m, 2H), 7.32 (q, *J* = 6.5 Hz, 2H), 7.20 (m_c, 2H), 5.79 (m_c, 2H), 2.91 (bs, 4H).

¹³C-NMR (DMSO-d₆) δ (ppm): 149.4 (d, *J* = 7.3 Hz), 149.3 (d, *J* = 7.1 Hz), 136.0, 135.9 132.7, 130.3, 129.5 (d, *J* = 3.6 Hz), 129.3 (d, *J* = 3.6 Hz), 128.4 (d, *J* = 2.2 Hz), 128.3 (d, *J* = 2.5 Hz), 125.4 (d, *J* = 1.6 Hz), 125.2 (d, *J* = 162 Hz), 124.3, 124.1 (d, *J* = 3.5 Hz), 124.0 (d, *J* = 3.5 Hz), 122.0, 121.8, 120.1 (d, *J* = 5.4 Hz), 120.0 (d, *J* = 5.0 Hz), 41.8, 41.7.

³¹P-NMR (DMSO-d₆) δ (ppm): 15.7, 15.6.

IR (ATR) ν (cm⁻¹) = 3159 (m), 2877 (w), 1598 (w), 1476 (m), 1446 (m), 1196 (s), 1146 (m), 1116 (s), 922 (s), 747 (s), 711 (m).

MS (ESI) m/z (%) 488 (100).

HR-MS (ESI-TOF) calculated for $[M+1]$ $C_{26}H_{23}N_2O_4P_2$ m/z 489.1128; found 489.1129

3. Results and Discussion

3.1 Comparison of different chlorinating agents

Seven different DOPO-based phosphoramidates were synthesized using three different chlorinating agents for the conversion of the P-H bond of DOPO into an intermediate P-Cl bond and subsequent reaction of the DOPO-Cl **3** derivative with respective amines. It can be seen from Table 1 that the appropriate amino-DOPO derivatives **4-10** could be synthesized in moderate to excellent yields depending on the chosen method and amines. In general method **B** provided the highest yields consistently whereas methods **A** and **C** are not efficient for all compounds. Using amines like benzylamine or propylamine bearing no additional functional group, all methods provide good to excellent yields up to 94% (Figure 1, entry 3, method **B**).

In case of glycine methylester, entry 5, product **8** was isolated in moderate yields of 30% and 59% respectively using method **A** and **C**. In contrast to that, method **B** was more efficient and led to a yield of 84% of **8**. Moreover the yields of **5**, **9**, and **10** were only moderate to good when method **C** was used. Lower yields for method **C** could be explained by a possible unfavorable interaction of cyanuric acid with the corresponding amine such as complex formation and subsequent precipitation. The reason for these lower yields was not investigated more in detail. Furthermore the chlorination reaction of DOPO with TCCA is quite exothermic even at small scale and thus for this method no reactions larger than 5 g was performed. The two bis-DOPO

compounds **9** and **10** could be isolated in very good yields between 83 and 85% when method **A** or **B** were applied.

The preparation of DOPO based phosphonamidates using CCl_4 has been described earlier for few compounds in lab scale experiments. But to the best of our knowledge no synthesis in a scale of > 1 mol, with regard to DOPO, has been reported so far. As described earlier in experimental section, EDA DOPO was prepared on a 500 g scale (based on DOPO weight). It is observed that both methods **A** and **B** work comparably well and provide the desired final product in a yield of 85% for method **A** and 83% respectively for method **B**. Due to a precipitation of the product from the reaction mixture the work up and isolation of the desired compounds is quite easy and efficient. These results indicate that both methods could be appropriate for up scaling of such phosphonamidate compounds. As CCl_4 is toxic and a proven carcinogen and its use is restricted in many countries, SO_2Cl_2 seems to be an efficient and attractive alternative reagent for the preparation of phosphonamidate compounds from phosphinites.

3.2 Thermal Stability

All synthesized amino DOPO derivatives were analyzed for their thermal stability using TGA. The TGA data could be useful in determining the suitability or possible further application of such compounds as flame retardant additive in different polymeric systems.

The TGA thermograms of mono DOPO derivatives **4-8** and unmodified DOPO are shown in Figure 1. It can be seen that the DOPO derivatives exhibit a significantly higher thermal stability as compared to DOPO itself. The onset of decomposition of DOPO starts at 237°C whereas its derivatives **4-8** are stable at this temperature. Thus by suitable choice of amine one can develop DOPO derivatives which are thermally more stable and suitable for different polymers. BA

DOPO **6** the highest thermal stability amongst the investigated mono DOPO derivatives. This higher thermal stability might be explained by a beneficial $\pi\pi$ interaction of the aromatic systems of DOPO and the additional benzyl group which could lead to a formation of more stable and less volatile conformers. The onset temperature of its decomposition was determined to be at 298.9 °C. **7** and **8** exhibit a comparable thermal stability of about 287.2 °C and 294.5 °C respectively. **4** and **5** seem to be the least stable of the investigated compounds with an onset temperature of 260 °C and 261 °C respectively. Amongst these mono DOPO derivatives Gly DOPO **8** is the only compound to leave a significant amount of residue at 700 °C, which is about 9.32%. The thermal decomposition of this compound proceeds via a two step mechanism. There is a relatively rapid and steep mass loss of about 20% (~220 °C – 280 °C) and after that the mass loss rate is significantly reduced until the final residue of 9.32% is reached. This residue and the slower mass loss rate in the second stage (~290 – 400 °C) could be explained by intermolecular condensation reactions of either the free N H group or the α carbon (type of Claisen Condensation) of one molecule with the ester group of another molecule.

The GA data of the two bis DOPO derivatives **9** and **10**, are presented in Figure 2. One can see that these compounds are thermally more stable than DOPO and other DOPO compounds **4–8**. The onset of the degradation of EDA DOPO **10** was measured to be 352 °C. PiP DOPO is even more stable with an onset temperature of 414 °C. A certain amount of residue was also detected for both compounds **9** and **10**, 4.07 and 5.2% respectively. The high thermal stability of **9** and **10** could be explained by a higher steric demand of these compounds. The two biphenyl moieties in these compounds can shield and protect the relatively labile P N bond and thus guarantee a higher thermal stability. In order to elucidate this hypothesis, we have carried out quantum chemical calculations. Therefore the geometry was optimized employing the dispersion corrected

ωB97xd functional and 6 311g+ basis set as implemented in the Gaussian09 suit of programs.¹⁷ This method is known to predict x ray structures with relatively small statistical errors for the overall geometry as well as selected bond length.¹⁸ Figure 3 shows the calculated structures of Gly DOPO (**8**), PiP DOPO (**9**) and EDA DOPO (**10**). Only the lowest energy conformers that were found are depicted. It becomes evident that steric shielding of the O=P group is more pronounced in **9** compared to **8** and **10**. The CH₂ group of the piperazin ligand (**9**) efficiently shields the backside of the O=P functional group. This might lead e.g. to a reduced reactivity of the O=P moiety towards nucleophilic attack and thus to a larger stability. However it does not explain the increased stability of EDA DOPO **10** compared with Gly DOPO **8**. Hence, we attribute this finding to association between neighboring molecules in the solid phase e.g. intermolecular forces. Both the higher shielding and the better organized structure in the solid phase supports a higher thermal stability. The corresponding melting points, onset temperatures and residues of all compounds presented in Table 2.

The high thermal stability and melting points of compound **9** and **10** could indicate that these compounds might be suitable and compatible with the processing conditions of polymers that are processed at elevated temperatures of >250 °C such as polyesters or polyamides. It can be additionally seen from Table 2 that the synthesized DOPO derivatives cover a wide range of melting areas. In contrast to the high melting bis DOPO compounds the mono compounds melt in a range between 95 °C and 156 °C. Due to such thermal characteristics these products could be interesting for application in lower melting polymers such as polyethylene, polypropylene or polyamide 12.

3.3 DIP-MS measurements

The availability of a flame retardant in the gas phase is an important criterion, which determines its efficacy and suitability for a polymeric system. It is usually assumed that the flame retardant should decompose and release active species in the gas phase at a temperature that is close to the degradation temperature of the polymer matrix. Thus DIP MS measurements were performed on the synthesized DOPO derivatives to evaluate the availability of the phosphorus species in gas phase at different temperatures. The total ion chromatogram of the mono DOPO derivatives is presented in Figure 4. Measurements with similar conditions on polyether based polyurethane foams can be found in literature.^{7c}

Like observed in TGA thermograms, DOPO **1** decomposes or volatilizes earlier as compared to its derivatives **4-8**. It starts to volatilize and decompose at around 2 minutes, which corresponds to a temperature of about 150 °C. The maximum decomposition rate is at around 2.5 minutes and after 3 minutes no more DOPO or its decomposition fragments can be detected. Compounds **4** and **5** start to volatilize at around 2.5 minutes and can be detected over relatively wide temperature range of about 50 °C. After 4 minutes no more **4**, **5** and their fragments can be detected. It was also noted in the TGA measurements that **7** and **8** volatilize and decompose in a similar temperature range. They can be detected starting from about 2.5 minutes and the maximum intensity can be observed at 4.1 and 4.2 minutes respectively. After 5 minutes no more fragments of these compounds can be detected. As expected from the TGA measurements **6** volatilizes and decomposes later than the other compounds. **6** and its decomposition fragments can be detected from 3.5 minutes until 5.5 minutes which corresponds to a temperature range of about 225 to 325 °C.

Both bis DOPO derivatives **9** and **10** volatilize and degrade at very high temperatures. EDA DOPO **10** and fragments of its decomposition can only be detected later than 7 minutes (Figure 5) which corresponds to a temperature of more than 350 °C. Only a very small amount of EDA could be detected below this temperature. Significant amounts of EDA DOPO can be observed between 9 and 10 minutes (temperature of 450 °C). PIP DOPO **9** is even more stable and less volatile because it can't be detected in the gas phase before 8.5 minutes(Figure 5).

Thus PIP DOPO **9** may be useful for polymers that degrade at higher temperatures such as 400 500 °C. Extracted MS data from TICs of the DOPO derivatives are given in the supporting information.

4. Conclusion

Seven different DOPO based phosphonamidates were successfully synthesized in moderate to excellent yields. Three different synthesis methods were used and compared with each other regarding yields of the products and also capability for up scaling trials. Method **A** (CCl₄) and **B** (SO₂Cl₂) were in general more efficient than method **C** (TCCA) due to higher yields and easier handling of the reaction process. Unlike in case of TCCA method, the reaction isn't exothermic for CCl₄ and SO₂Cl₂ methods and thus EDA DOPO **10** was prepared on a 500g scale (> 2mol) in the lab. Such synthetic methods for synthesis of phosphonamidates could be suitable for future scale up at industrial level. The thermal stabilities and volatilities (gas phase availability) of the synthesized compounds were investigated by TGA and DIP MS. All DOPO derivatives were much more thermally stable than unmodified DOPO. Amongst mono DOPO derivatives, BA DOPO **6** exhibits the highest thermal stability and is only superseded by bis DOPO derivatives **9** and **10**. These compounds exhibit a thermal stability greater than > 300 °C , which makes them

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3 interesting as flame retardant additives for application in for polymer which have high melt
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■ Associated Content

Supporting Information

General procedures of all small scale reactions are given as supporting information. Analytical data including copies of NMR and DIP-MS are also given as supporting information free of charge via the Internet at <http://pubs.acs.org/>.

■ ACKNOWLEDGEMENTS

The authors thank the EMPA Postdocs program, (co-funded by the FP7, People Marie-Curie action “COFUND”) for financial support. Finally the authors are very thankful to Mrs. Elisabeth Michel for her help in series of analytical measurements. DFT calculations were performed at the HPC cluster Merlin4 located at Paul Scherrer Institute.

■ REFERENCES

1. (a) Quin, L. D., *A Guide to Organophosphorus Chemistry*. 2000; (b) Westheimer, F. H., *Sciences* **1987**, 235, 1173-1178; (c) Cherkasov, R. A., *Tetrahedron* **1985**, 41, 2567-2624.
2. (a) Li, Z. R., *Bioorganic & medicinal chemistry* **2003**, 11, 4171-4178; (b) Levchik, S. V., *Advances in fire retardant materials*. 2008; (c) Levchik, S. V., *Journal of fire sciences* **2004**, 22, 25 40; (d) Liu, W., *Polymer* **2007**, 48, 2345 2354; (e) Rakotomalala, M., *Materials* **2010**, 3, 4300 4327; (f) Warner, V. D., *Journal of medicinal chemistry* **1973**, 16, 1185 1186.
3. Meerts, I.; Letcher, R. J.; Hoving, S.; Marsh, G.; Bergman, A.; Lemmen, J. G.; van der Burg, B.; Brouwer, A., In vitro estrogenicity of polybrominated diphenyl ethers, hydroxylated PBDEs, and polybrominated bisphenol A compounds. *Environmental Health Perspectives* **2001**, 109 (4), 399 407.

4. Robrock, K. R.; Korytár, P.; Alvarez-Cohen, L., Pathways for the Anaerobic Microbial Dehalogenation of Polybrominated Diphenyl Ethers. *Environmental Science & Technology* **2008**, 42 (8), 2845-2852.
5. Boon, J. P.; Lewis, W. E.; Tjoen-A-Choy, M. R.; Allchin, C. R.; Law, R. J.; de Boer, J.; ten Hallers-Tjabbes, C. C.; Zegers, B. N., Levels of Polybrominated Diphenyl Ether (PBDE) Flame Retardants in Animals Representing Different Trophic Levels of the North Sea Food Web. *Environmental Science & Technology* **2002**, 36 (19), 4025-4032.
6. (a) Chen, L.; Song, L.; Lv, P.; Jie, G.; Tai, Q.; Xing, W.; Hu, Y., A new intumescent flame retardant containing phosphorus and nitrogen: Preparation, thermal properties and application to UV curable coating. *Progress in Organic Coatings* **2011**, 70, 59-66; (b) Gaan, S.; Mauclair, L.; Rupper, P.; Salimova, V.; Tran, T.-T.; Heuberger, M., Thermal degradation of cellulose acetate in presence of bis-phosphoramidates. *Journal of Analytical and Applied Pyrolysis* **2011**, 90, 33-41; (c) Gaan, S.; Rupper, P.; Salimova, V.; Heuberger, M.; Rabe, S.; Vogel, F., Thermal decomposition and burning behavior of cellulose treated with ethyl ester phosphoramidates: Effect of alkyl substituent on nitrogen atom. *Polymer Degradation and Stability* **2009**, 94, 1125-1134; (d) Tsafack, M. J.; Levalois-Grützmaier, J., Flame retardancy of cotton textiles by plasma-induced graft-polymerization (PIGP). *Surface and Coatings Technology* **2006**, 201, 2599-2610.
7. (a) Calzia, K. J.; Forcum, A.; Lesser, A. J., Comparing reinforcement strategies for epoxy networks using reactive and non-reactive fortifiers. *Journal of Applied Polymer Science* **2006**, 102, 4606-4615; (b) Nguyen, C.; Jinhwan, K., Synthesis of a Novel Nitrogen-Phosphorus Flame Retardant Based on Phosphoramidate and Its Application to PC, PBT, EVA, and ABS. *Macromolecular Research* **2008**, 16, 620-625; (c) Neisius, M.; Liang, S.; Mispereuve, H.; Gaan, S., Phosphoramidate-Containing Flame-Retardant Flexible Polyurethane Foams. *Industrial & Engineering Chemistry Research* **2013**, 52 (29), 9752-9762; (d) Liang, S.; Neisius, M.; Mispereuve, H.; Naescher, R.; Gaan, S., Flame retardancy and thermal decomposition of flexible polyurethane foams: Structural influence of organophosphorus compounds. *Polymer Degradation and Stability* **2012**, 97, 2428-2440.
8. (a) Xalter, R.; Roth, M.; Doering, M.; Michael, C.; Wagner, S. P-N compounds as flame retardants in polymer compositions. WO2013068437A2 2013; (b) Gaan, S.; Neisius, M.; Mercoli, P.; Liang, S.; Mispereuve, H.; Naescher, R. Phosphoramidates, production methods and flame retardant applications. WO2013020696A2, 2013; (c) Dumitrascu, A.; Howell, B. A., Flame retardant polymeric materials achieved by incorporation of styrene monomers containing both nitrogen and phosphorus. *Polym. Degrad. Stab.* **2012**, 97 (12), 2611-2618; (d) Wagner, S.; Rakotomalala, M.; Bykov, Y.; Walter, O.; Doering, M., Synthesis of new organophosphorus compounds using the Atherton-Todd reaction as a versatile tool. *Heteroat. Chem.* **2012**, 23 (2), 216-222; (e) Bykov, Y.; Wagner, S.; Walter, O.; Doering, M.; Fischer, O.; Pospiech, D.; Koeppl, T.; Altstaedt, V., Synthesis of new dibenzo[c,e][1,2]oxaphosphorine 2-oxide containing diols based on diethanolamine. *Heteroat. Chem.* **2012**, 23 (2), 146-153; (f) Artner, J.; Ciesielski, M.; Ahlmann, M.; Walter, O.; Döring, M.; Perez, R. M.; Altstädt, V.; Sandler, J. K. W.; Schartel, B., A Novel and Effective Synthetic Approach to 9,10-Dihydro-9-oxa-10-phosphaphenanthrene-10-oxide (DOPO) Derivatives. *Phosphorus, Sulfur, and Silicon and the Related Elements* **2007**, 182 (9), 2131-2148.
9. (a) Koenig, A.; Kroke, E., Flame retardancy working mechanism of methyl-DOPO and MPPP in flexible polyurethane foam. *Fire and materials* **2012**, 36 (1), 1-15; (b) Koenig, A.; Kroke, E., Methyl-DOPO-a new flame retardant for flexible polyurethane foam. *Polymers for*

- advanced technologies* **2011**, 22 (1), 5 13; (c) Granzow, A., Flame retardation by phosphorus compounds. *Accounts of Chemical Research* **1978**, 11 (5), 177 183; (d) Lefebvre, J.; le Bras, M.; Bastin, B.; Paleja, R.; Delobel, R., Flexible Polyurethane Foams: Flammability. *Journal of Fire Sciences* **2003**, 21 (5), 343 367.
10. Waaijers, S. L.; Hartmann, J.; Soeter, A. M.; Helmus, R.; Kools, S. A. E.; de, V. P.; Admiraal, W.; Parsons, J. R.; Kraak, M. H. S., Toxicity of new generation flame retardants to *Daphnia magna*. *Sci. Total Environ.* **2013**, 463-464, 1042-1048.
11. Liang, S.; Neisius, M.; Mispereuve, H.; Naescher, R.; Gaan, S., Flame retardancy and thermal decomposition of flexible polyurethane foams: Structural influence of organophosphorus compounds. *Polymer Degradation and Stability* **2012**, 97 (11), 2428-2440.
12. (a) Atherton, F. R.; Openshaw, H. T.; Todd, A. R., 174. Studies on phosphorylation. Part II. The reaction of dialkyl phosphites with polyhalogen compounds in presence of bases. A new method for the phosphorylation of amines. *Journal of the Chemical Society (Resumed)* **1945**, (0), 660-663; (b) Georgiev, E. M.; Kaneti, J.; Troev, K.; Roundhill, D. M., An ab initio study of the mechanism of the Atherton-Todd reaction between dimethyl phosphonate and chloro- and fluoro-substituted methanes. *J. Am. Chem. Soc.* **1993**, 115, 10964-73; (c) Troev, K.; Kirilov, E. M. G.; Roundhill, D. M., A study of the Atherton-Todd reaction mechanism. *Bull. Chem. Soc. Jpn.* **1990**, 63, 1284-5; (d) Kong, A.; Engel, R., A mechanistic investigation of the Todd reaction. *Bull. Chem. Soc. Jpn.* **1985**, 58, 3671-2.
13. (a) Ábrányi-Balogh, P.; Keglevich, G., Practical Synthesis of 6-Chloro-dibenzo[c.e][1,2]oxaphosphorine. *Synthetic Communications* **2011**, 41 (10), 1421-1426; (b) Kerenyi, A.; Balassa, A.; Kortvelyesi, T.; Ludanyi, K.; Keglevich, G., Synthesis and complexation of novel dibenzo[c.e][1,2]oxaphosphorine-based P-ligands. *Transition Met. Chem. (Dordrecht, Neth.)* **2008**, 33 (4), 459-465; (c) Keglevich, G.; Szelke, H.; Kerenyi, A.; Kudar, V.; Hanusz, M.; Simon, K.; Imre, T.; Ludanyi, K., New chiral P-ligands: P-amino- and P-cycloalkoxy dibenzo[c.e][1,2]oxaphosphorines. *Tetrahedron: Asymmetry* **2005**, 16 (24), 4015-4021.
14. (a) Su, W.-C.; Sheng, C.-S. Method for preparing a biphenylphosphonate compound useful as flame retardant. US20050101793A1, 2005; (b) Ando, S.; Imamura, K.; Tanabe, S.; Taketani, Y. Preparation of pentaerythritol spirocyclic bis(phosphonate)s without drying of the bis(hydrophosphonate) intermediate and isolation of the alkali salt intermediates. JP2004035481A, 2004.
15. Acharya, J.; Gupta, A. K.; Shakya, P. D.; Kaushik, M. P., Trichloroisocyanuric acid: an efficient reagent for the synthesis of dialkyl chlorophosphates from dialkyl phosphites. *Tetrahedron Lett.* **2005**, 46 (32), 5293-5295.
16. (a) Mundy, J. L.; Harrison, J. M.; Watts, P.; Timperley, C. M., Isotopically labelled phosphorus compounds: some deuterated methyl and ethyl derivatives. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006**, 181 (8), 1847-1857; (b) Liao, X.; Anjaneyulu, P. S. R.; Curley, J. F.; Hsu, M.; Boehringer, M.; Caruthers, M. H.; Piccirilli, J. A., The Tetrahymena ribozyme cleaves a 5'-methylene phosphonate monoester ~102-fold faster than a normal phosphate diester: Implications for enzyme catalysis of phosphoryl transfer reactions. *Biochemistry* **2001**, 40 (37), 10911-10926.
17. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.;

1
2
3 Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.;
4 Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.;
5 Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene,
6 M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R.
7 E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.;
8 Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.;
9 Daniels, A. D.; Farkas; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., Gaussian 09,
10 Revision B.01. Wallingford CT, 2009.
11
12

13 18. Minenkov, Y.; Singstad, A.; Occhipinti, G.; Jensen, V. R., The accuracy of DFT
14 optimized geometries of functional transition metal compounds: a validation study of catalysts
15 for olefin metathesis and other reactions in the homogeneous phase. *Dalton Transactions* **2012**,
16 41 (18), 5526 5541.
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Scheme 1. General scheme for Atherton-Todd reaction for preparation of phosphoramidates

Scheme 2. Two-step reaction procedure involving H₂O₂ as oxidizing agent

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Scheme 3. General reaction scheme for the preparation of phosphoramidates using three different chlorinating agents

Entry	Nu =	Product ^a	(A) CCl ₄ ^b	(B) SO ₂ Cl ₂ ^c	(C) TCCA ^d
1		PA-DOPO <u>4</u>	89	89	83
2		AA-DOPO <u>5</u>	88	88	61
3		BA-DOPO <u>6</u>	89	94	90
4		MeO-DOPO <u>7</u>	81	81	91
5		Gly-DOPO <u>8</u>	30	84	59
6		PiP-DOPO <u>9</u>	85	83	56
7		EDA-DOPO <u>10</u>	84	85	74

a) 5g DOPO was used as reactant for each reaction; 1.1 eq. of Et₃N were used as base; b) CH₂Cl₂ was used as solvent, 1.1 eq. of CCl₄ were used; c) CH₂Cl₂ was used as solvent, 1.005 eq. of SO₂Cl₂ were used; d) acetonitrile was used as solvent, 0.34 eq. of TCCA were used.

Table 1: Reaction yield of various phosphonamidates

<i>Compound</i>	<i>T_{Onset} (°C)</i>	<i>M_{residual at 700 °C} (%)</i>	<i>T_{melting} (°C)</i>
1	237	1.4	119-121°C
4	260	1.8	127 °C
5	261	2.6	95 °C
6	299	2.4	156 °C
7	287	2.1	113 °C
8	295	9.3	126 °C
9	414	5.2	>300 °C
10	352	4.1	272 °C

Table 2. Onset temperatures and residual mass determined by TGA and melting points

Figure 1. TGA curves of mono-DOPO derivatives **4-8** in comparison with DOPO **1**

Figure 2. TGA curves of bis-DOPO derivatives **9-10** in comparison with DOPO **1**

Gly-DOPO (8)

PIP-DOPO (9)

EDA-DOPO (10)

Figure 3. Computed structures of Gly-DOPO (8), PiP-DOPO (9) and EDA-DOPO (10)

Figure 4. Total ion Chromatogram (TIC) of mono-DOPO derivatives **4-8** in comparison with DOPO **1**

Figure 5. Total ion Chromatogram (TIC) of bis-DOPO derivatives **9-10** in comparison with DOPO **1**