The Use of 2,4,6-Tris(4-methoxyphenyl)-1,3,5,2,4,6-trioxatriphosphinane 2,4,6-trisulfide (TMPT) as a Novel Imide and *N*-Sulfonylcarboxamide Thionating Agent

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Introduction

Transformation of carbonyl containing compounds such as amides and imides into their sulfur containing analogues is an important synthetic tool in organic chemistry. A number of reagents such as Lawesson's reagent 1 (2,4-bis(4-methoxyphenyl)-2,4-dithioxo-1,3,2,4-dithiaphosphetane), phosphorous pentafluoride, and elemental sulfur are commonly used. We are exploring the use of another novel thionating reagent 2,4,6-tris(4-methoxyphenyl)-1,3,5,2,4,6-trioxatriphosphinane 2,4,6-trisulfide which is abbreviated as TMPT 2. TMPT was well characterized earlier in our lab by ^{1}H NMR spectroscopy and by single crystal X ray crystallography. In earlier work we have demonstrated TMPT converts a variety of amides into their corresponding thioamides. In this current project we are focusing on expanding the utility of TMPT to the thionation of cyclic imides and sulfonylcarboxamides. The cyclic imides have two potential sites for thionation resulting in mono- and di-substituted products. Several of the cyclic imides and the sulfonylcarboxamides have low solubility in refluxing toluene with TMPT.

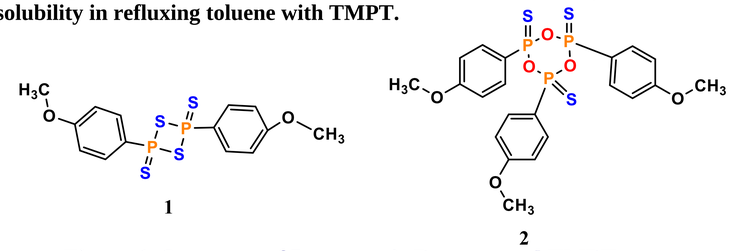

Figure 1. Structure of Lawesson's Reagent and TMPT

Phthalimide 3 was reacted with TMPT (figure 2) under two different reaction conditions noted in Table 1.
Very low solubility of 3 in toluene promoted the change to the more polar solvent pyridine. The products 4 and 5 were identified by compound color, TLC polarity, and melting point.

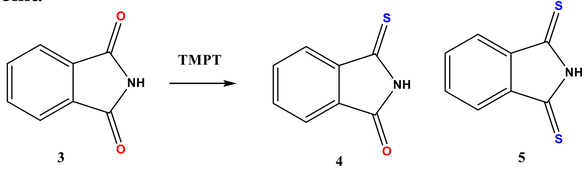

Figure 2 Reaction of Phthalimide with TMPT

Table 1 Reaction Conditions of Phthalimide and TMPT

TMPT equivalence	Conditions	4, % yield	5, %yield
0.33	Refluxing toluene 14 h	0	4
0.33	Refluxing Pyridine 11 h	28	25

Alternative solvents were examined in order to optimized the thionation reaction conditions (Table 2). Thionation of benzamide 6 was attempted using acetonitrile and tetrahydrofuran (THF). Under refluxing acetonitrile conditions compound 7 was produced in a good yield whereas the boiling point of THF was not sufficient to activate TMPT 1 (figure 3).

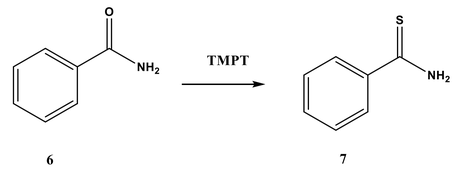

Figure 3 Reaction of Benzamide with TMPT

Table 2 Reaction Conditions of Benzamide 6 and TMPT

TMPT equivalence	Conditions	7 % yield
0.33	Refluxing toluene 6 h	73
0.66	Refluxing acetonitrile 7 h	73
0.66	Refluxing THF	0

Similar reaction conditions were used to thionate compound 8 in good yield (Figure 4).

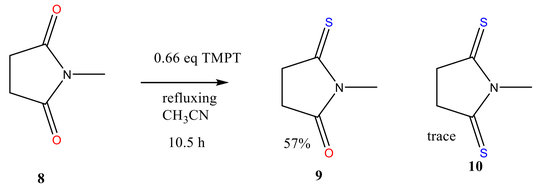

Figure 4 Reaction of N-methyl succimide 8 with TMPT

Figure 5 ^{1}H NMR Spectrum of 9

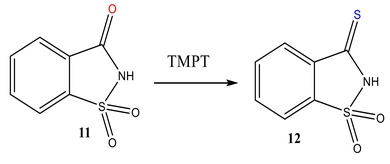

Figure 6 Reaction of saccharin with TMPT

Conclusion

- **Successfully thionated aromatic and aliphatic cylic imides with TMPT in moderate yields.**
- **Identified alternate solvent for TMPT thionation reactions.**
- **Attempts to thionate saccharine resulted in complex mixture of products which will be need to be purified further.**

Future Work

- **Expand the investigations with more imides for structural diversity.**
- **Explore mechanistic studies**

Acknowledgements

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Experimental Methods

Synthesis of TMPT 1
To a 100mL round bottom flask equipped with a water-cooled condenser was added Lawesson's Reagent (0.5 eq. 1.06g, 2.6 mmol) and Toluene (30mL). The solution turned a yellow color upon heating with most of the Lawesson's reagent going into solution. The reaction mixture was refluxed for 16 hours. When reaction cooled to room temperature, a white solid precipitated which identified as Lawesson's reagent by TLC. The white solid was removed by filtration and dried in a desiccator to yield 0.4925 g of Lawesson's reagent. The filtrate was added and concentrated *in vacuo* to yield .5557g. The product was purified by column chromatography hexanes and ethyl acetate, 4:1) to yield 0.50127 g of a white solid **1.**

Synthesis of thiobenzamide 7
To a 50 mL bottom flask equipped with condenser was added benzamide (54 mg, 0.45 mmol), TMPT (158.9 mg, 0.279 mmol) and acetonitrile (10 mL). The reaction mixture was refluxed for 7 hours until all the starting benzamide was consumed as indicated by TLC. The reaction was concentrated in a vacuum to yield a yellow solid which was purified by column chromatography (eluent 3/1 hexanes/EtOAc) to 53 mg of thiobenzamide. (73% yield) and a melting point of 115.2 - 116.5°C.

Synthesis of 1-methyl-5-thioxopyrrolidin-2-one
To a 50 mL bottom round flask equipped with condenser was added N-methylsuccinimde (54mg, 0.479 mmol), TMPT (176mg, 0.316 mmol) and toluene(10 mL). The reaction mixture was refluxed for 10 hours 30 minutes until all the starting N-methylusccinimide was consumed as indicated by TLC. The reaction was concentrated in a vacuum to yield a yellow solid which was purifed by column chromatography with solvent system of 3/1 hexanes/EtOAc. 155-156.7 m.p.

Synthesis of thiosaccharin 12
To a 50 mL bottom round flask equipped with condenser was added saccharin (93mg, 0.508 mm/mol). TMPT (188 mg, 0.33 mm/mol) and acetonitrile (10 mL). The reaction mixture was refluxed for 6 hours and 34 minutes until all the starting saccharin was consumed as indicated by TLC. The reaction was concentrated in a vacuum to yield a yellow solid which was purified by column chromatography with solvent system of 2:1 hexane/EtOAc to 65 mg of thiosaccharin and melting point of yellow solid was 104.0°C and white solid was 58.6°C