



Synthesis of P-isopropylacetate-N-methyl-1,3,5-triaza-7-phosphaadamantane

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Abstract A novel phosphine, *p*-isopropylacetate *N*-methyl-1,3,5-triaza-7-phosphaadamantane, has been synthesized as a triflate salt from the reaction of 1,3,5-triaza-7-phosphaadamantane with methyl triflate in dry acetone in the presence of minimal amount of D₂O and triflic acid. The compound was characterized by NMR spectroscopy, IR spectroscopy, and mass spectrometry. It was crystallized as the triflate salt, [C₁₃H₂₆N₃OP]²⁺ 2[CF₃SO₃]⁻, **1**, with two molecules of anions, which was characterized by X-ray crystallography. The geometry about the phosphorus center has been found to be slightly distorted tetrahedral. The proposed mechanistic pathway for the formation of the compound **1** consists of formation of a condensation product, nucleophilic attack by phosphorus, and N-methylation.

Keywords TPA-derivative, *N*-methyl-1,3,5-triaza-7-phosphaadamantane, tertiary phosphine, triazacyclohexane

Introduction

A number of open-cage derivatives of one of the widely used tertiary phosphine ligands in recent days, TPA or PTA, (TPA = 1,3,5-triaza-7-phosphaadamantane), can be synthesized from triazacyclohexane ring by C-N bond cleaving [1-3]. Diacetyl derivative of TPA, called DATPA or DAPTA (DATPA = *N,N'*-diacetyl-1,3,5-triaza-7-phosphaadamantane) is known and its crystal structure has recently been reported [1]. The steric behavior of a phosphine ligand, which attributes to its coordination chemistry, can be described in terms of Tolman's cone angle [4]. Reaction of TPA with CH₃OTf (OTf = CF₃SO₃⁻) in 1:2 molar ratio in dry acetone has led to the formation of a water-soluble bis-methylated TPA-derivative on its lower rim [5]. As a result of such reaction, dicationic derivative of this ligand; *N,N'*-dimethyl-1,3,5-triaza-7-phosphadamantane as the triflate salt, resembling the cone angle and electronic properties to TPA, was formed. The solubility of this compound in water was found to be 12 mg/ml at 25 °C [5]. A number of metal complexes of the TPA-derivatized ligands are only slightly soluble in common organic solvents and water. Therefore, their coordination chemistry still remains unexplored [6-7].

For this reason, there is a need of synthesis of new TPA-derivative phosphine compounds that is soluble in water and/or other common solvents as well as serves as a ligand; especially for the lower valence metal complexes [6]. It would be a quite interesting study to investigate the coordination chemistry of such complexes and explore their catalytic as well as numerous other properties. The water-soluble catalysts will also possess the potential applications in biphasic catalytic system [3b]. In this regard, synthesis and characterization of a novel water-soluble TPA-derivative compound, *P*-isopropylacetate *N*-methyl-1,3,5-triaza-7-phosphaadamantane triflate (**1**), has been reported herein for the first time.



Materials and Method

General Comments: Unless otherwise indicated, the reactions were performed under an inert atmosphere of nitrogen using dried glassware on a dual-manifold Schlenk line. Unless otherwise stated, all solvents were of ACS reagent grade quality. The solvents were purchased from Pharmco-Aaper Co. and used as received, unless otherwise mentioned. All other chemicals were purchased from Sigma Aldrich Chemical Co. Triflic acid and dimethyl sulfoxide (DMSO)- d_6 were dried over activated 4Å molecular sieves for at least 24 h prior to use and D_2O was used as received. Acetone was dried over anhydrous $MgSO_4$ for 12 h and placed over activated 4Å molecular sieves for 24 h.

NMR spectra were recorded on Bruker Avance-400 MHz spectrometers at ambient temperature. Spectroscopic data were recorded at 400, 100 and 161 MHz, respectively, for 1H , $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR experiments. Proton, carbon and phosphorus chemical shifts (δ) were reported relative to the residual deuterated solvent, and external H_3PO_4 resonances, respectively. Chemical shifts were reported in parts per million (ppm) and coupling constants (J) in Hertz (Hz). IR spectra were measured as a KBr disc using a MIDAC Corporation M-Series FTIR spectrometer. Mass spectrometric analysis was carried out on Hewlett-Packard 5989A Mass Spectrometer calibrated with NaI. Melting points were measured in a sealed capillary tube using a Mel-Temp apparatus equipped with a 500 °C thermometer.

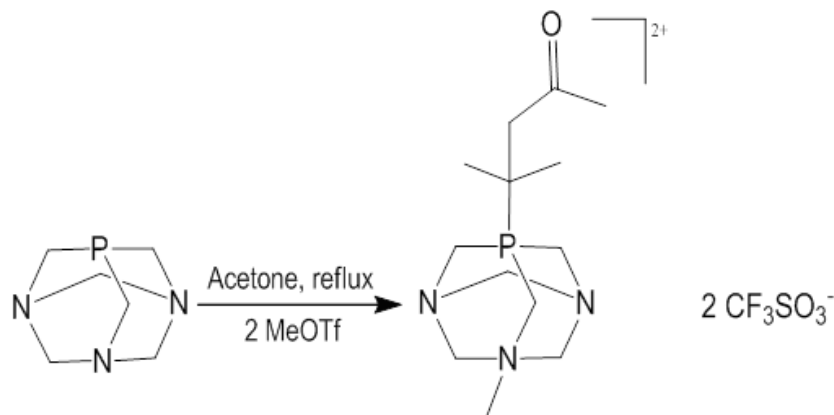
Synthesis of 1: TPA (0.252 g, 1.60 mmol) was placed in a 50 ml two-necked round bottom flask fitted to the Schlenk-line. To 30 ml of dry acetone in a closed flask, 2 drops of D_2O was added through a syringe. Then this acetone was transferred into the flask through a syringe. The mixture was stirred at ambient temperature to dissolve the TPA completely. Triflic acid (0.016 g, 0.052 mmol) was added to this solution followed by methyl triflate (0.570 g, 3.22 mmol). The resulting solution, with continuous stirring, was refluxed for 4 h under nitrogen atmosphere and then cooled at room temperature slowly. The reaction mixture was then placed at -10 °C for 6 h. Then 7 ml of carbon tetrachloride was added to this cold solution. A white precipitate was formed which was filtered through a sintered glass frit. The residue was washed with 3 ml of *n*-hexane and dried *in vacuo*. Compound **1** was obtained as a white solid (0.692 g, 76% yield), Mp 277-280 °C. Single crystals of **1** were obtained after 72 h when the solution of **1** in *n*-hexane and acetone (1:1) was cooled at -20 °C. 1H NMR (400 MHz, DMSO- d_6): δ 5.11 (b, 4H, NCH_2NC), 4.97 (d, J = 9.0 Hz, 2H, NCH_2N), 4.79-4.62 (m, 4H, PCH_2N), 4.43 (dd, J = 45.0 Hz, 13.8 Hz, 2H, PCH_2NC), 3.15 (d, J = 21.0 Hz, 2H, CH_2), 2.87 (d, J = 6.3 Hz, 3H, NCH_3), 2.22 (s, 3H, $COCH_3$), 1.32 (d, J = 19.2 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO- d_6): δ 206.4 (CO), 120.3 (q, J = 315 Hz, CF_3), 77.6 (NCH_2NC), 76.9 (NCH_2N), 53.6 (d, J = 32.2 Hz, PCH_2NC), 51.7 (NCH_3), 45.1 (d, J = 28.5 Hz, PCH_2N), 42.1 (d, J = 22.5 Hz, CH_2), 32.9 (d, J = 22.5 Hz, C), 30.5 ($COCH_3$), 21.2 (CH_3). $^{31}P\{^1H\}$ NMR (161 MHz, DMSO- d_6): δ -14.1. MS: m/z (%) 717 (100), 633 (43), 420 (98), 336 (37), 270 (90), 227 (51). HRMS: m/z Calcd for $C_{15}H_{26}N_3O_7F_6PS_2$, 569.0854; Found: 569.0859 (M^+). IR (KBr, cm^{-1}): ν 1615 (C=O).

X-ray crystallography: The instrument used was a Bruker SMART 1000 diffractometer, using Mo- K_α radiation and equipped with cryostream [8]. Crystals were mounted on glass fibers using paratone oil. Data collection and data reduction were carried out using Bruker SAINT using a narrow frame algorithm and SADABS [9] was run for absorption correction on all data. All structures were solved by direct methods and subsequent difference Fourier syntheses and refined by full matrix least-squares methods against F^2 (SHELX 97) [10-11].

Results and Discussion

Compound **1** was synthesized by heating a mixture of TPA and methyl triflate in 1:2 molar ratio for 4 h in dry acetone in the presence of a minimal quantity of D_2O and triflic acid followed by cooling the reaction mixture at -10 °C (**Scheme 1**). It was obtained in 76% yield as a white solid. Formation of *N,N'*-dimethylTPA triflate has been reported from similar reaction in dry acetone [5]; however, use of dry acetone at abovementioned conditions under reflux led to the formation of **1** in a very good NMR yield (isolated yield).





Scheme 1: Synthesis of $[C_{13}H_{26}N_3OP]^+ 2[CF_3SO_3]^-$, **1**.

Spectral analysis of **1** in the 1H NMR spectroscopy exhibited a single resonance corresponding to the acetyl hydrogen at $\delta = 2.22$ and broad signal corresponding to the NCH_2NC hydrogen at $\delta = 5.11$. The magnetically non-equivalent PCH_2NC protons were diagnostic by the appearance of a doublet of doublets peak at 4.43 ppm with the coupling constant (J) values 45.0 and 13.8 Hz. Diagnostic to the NCH_2N , CH_2 , NCH_3 , and CH_3 protons, four doublets were observed at 4.97 ($J = 15.0$ Hz), 3.15 ($J = 21.0$ Hz), 2.86 ($J = 6.3$ Hz), and 1.30 ($J = 19.2$ Hz) ppm, respectively. Furthermore, in agreement with the PCH_2N hydrogen, a multiple resonances appeared around 4.70 ppm due to multiple coupling with neighboring protons and phosphorus.

The $^{31}P\{^1H\}$ NMR spectral analysis of **1** in $DMSO-d_6$ showed a downfield resonance at $\delta = -14.1$ (compared to -81.7 for N,N' -dimethylTPA triflate) [5], as a result of stronger deshielding due to the presence of the acetyl group in the former [12]. The splitting patterns of the spectra in the 1H and $^{13}C\{^1H\}$ NMR reported for N,N' -dimethylTPA triflate [5] and that observed for **1** were found to be identical. As observed from the proton-decoupled ^{13}C NMR spectra of **1**, couplings of ^{13}C underwent with other NMR active nuclei; ^{31}P and ^{19}F .

This method resulted in reproducible reactions with a better yield as well as better X-ray diffraction quality single crystals of **1** compared to the previous attempts employing different reaction conditions in which D_2O and triflic acid were not applied and commercially available acetone was used as received [13]. This is possibly due to formation of undesired condensation products via excessive hydrolysis and not following the proposed reaction path by the reaction during those attempts.

Single crystal of **1** was obtained after 72 h by cooling its solution in n -hexane and acetone (1 : 1) at $-20^\circ C$. It was crystallized as triclinic crystal system in a P-1 space group (Table 1). The phosphine crystal also consists of two molecules of triflate ($CF_3SO_3^-$) counter-anion and a solvent (acetone) molecule.

Table 1: Crystal data for $[C_{13}H_{26}N_3OP]^+ 2[CF_3SO_3]^- \cdot CH_3COCH_3$ molecule

$Mr = 627.14$	$V = 1313.26 (10) \text{ \AA}^3$
$D = 1.584 \text{ g/cm}^3$	$Z = 2$
$a = 8.2445(2) \text{ \AA}$	$\lambda = 0.76 \text{ \AA}$
$b = 10.3582(6) \text{ \AA}$	$\mu = 0.46 \text{ mm}^{-1}$
$c = 16.4755(6) \text{ \AA}$	$T = 110 \text{ K}$
$\alpha = 108.059(2)^\circ$	$\theta_{\text{max}} = 27.6^\circ$
$\beta = 99.716(3)^\circ$	$R = 0.0506$
$\gamma = 91.297(4)^\circ$	$wR_2 = 0.1327$

The unit cell consists of two solvent and four $CF_3SO_3^-$ molecules which are packed into layers, each consisting of a molecule of cation and solvent as well as two molecules of anion. The geometry around P-center is tetrahedral; however, it is distorted to some extent around the adamantane cage (Figure 1).



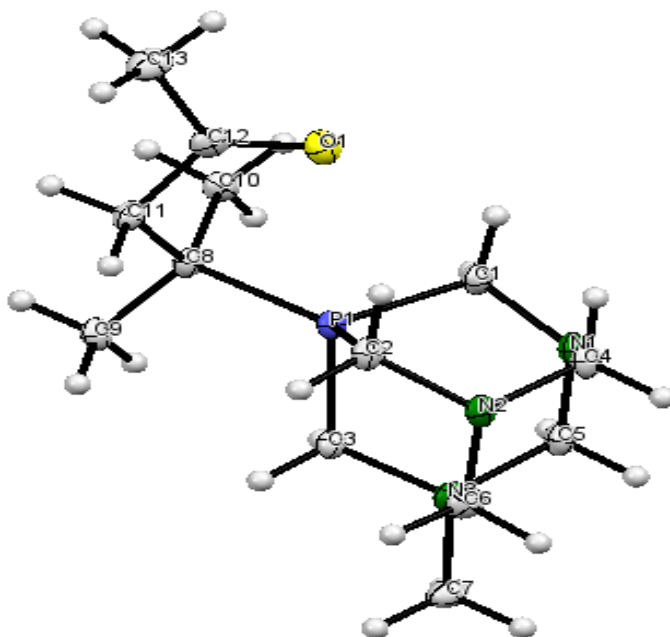
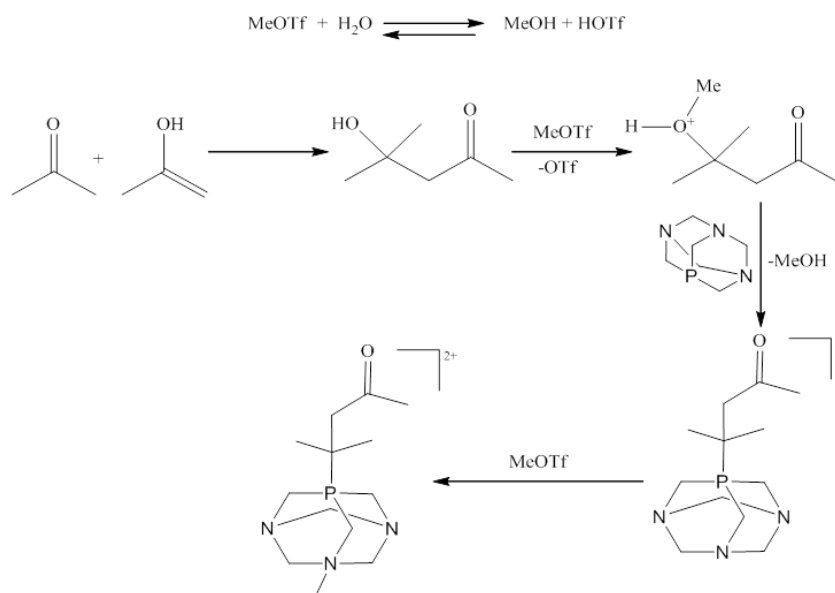


Figure 1: ORTEP diagram for **1** (50% probability ellipsoids). Anion molecules have been omitted for clarity. Selected bond lengths and bond angles are mentioned in **Table 2**. The C8–P1–C3 bond angle [$108.7(2)^\circ$] closely resembles the standard tetrahedral angle. The C8–P1–C1 and C8–P1–C2 angles are $117.8(3)^\circ$ and $122.5(2)^\circ$, respectively. The P1–C8 bond [$1.849(2) \text{ \AA}$] is slightly longer than a typical P–C bond and closer to the P–C bond length reported for *N,N'*-dimethylTPA ligand [$1.840(5) \text{ \AA}$] [5]. The structure contains a methylated nitrogen with the P-atom bound to 4-methylpentan-2-one. Therefore, use of **1** as a *P*-donor ligand seems less likely, but as reported in few literatures [6, 14], it could still be utilized as an *N*-donor ligand.

Table 2: Selected bond lengths and bond angles for the compound **1**

C11–C12	P1–C8	C8–P1–C3	C8–P1–C2	C8–P1–C1	C7–N3–C5	N3–C5	C=O	N1–C1
1.507(4)Å	1.849(2)Å	108.7(2) $^\circ$	122.5(2) $^\circ$	117.8(3) $^\circ$	109.5(1) $^\circ$	1.543(3)Å	1.226(5)Å	1.461(6)Å



Scheme 2: Proposed mechanism for the synthesis of **1**



As described in literature [15], it appears that the C–N bond lengths are the most affected upon alkylation of the TPA nitrogen. Therefore, the C–N bond distances for the unsubstituted N-atom are close to the average C–N bond length of TPA [1.463(4)Å] [15]. The geometry about the methylated nitrogen is nearly tetrahedral, all the C–N–C bond angles lying in the range of 107.5(1)° to 110.4(1)°; which closely resemble the tetrahedral angles. The C=O bond distance of the acetyl group is 1.226(5)Å; comparable to that of DATPA (1.224Å) [15]. The C12–C13 [1.493(2)Å] and C11–C12 [1.507(4)Å] bonds are significantly shorter than the typical C–C bond (1.54Å) which could be attributed to inductive effect and/or the molecule's existence in its 'enol' tautomer partially.

The mechanism for formation of **1** is still seems to be elusive; however, it has been anticipated that added triflic acid and that formed by possible hydrolysis of methyl triflate promotes keto-enol tautomerism of acetone in the presence of D₂O [16-17] (**Scheme 2**). The 'enol' form gives a condensation product, 4-hydroxy-4-methylpentan-2-one, after reacting with the 'keto' form. The hydroxy compound gets methylated from another molecule of methyl triflate. This is followed by nucleophilic attack by phosphorus and finally, *N*-methylation.

Conclusion

A novel water-soluble TPA-derivative compound, *P*-isopropylacetate *N*-methyl-1,3,5-triaza-7-phosphaadamantane cation has been synthesized as a triflate salt by the reaction of 1,3,5-triaza-7-phosphaadamantane and methyl triflate in dried acetone in the presence of minimal amount of D₂O and triflic acid. Single crystal structure of the compound was analyzed by X-ray crystallography and it showed that the geometry about the phosphorus center was found to be nearly tetrahedral. The unit cell consists of layers; each consists of a cation molecule, two molecules of anion, and an acetone molecule that has been used as a solvent. The possible mechanism for formation of this phosphine salt has been proposed; in which the formation of the product is primarily caused by tautomerism. It would be quite interesting to investigate its reactivity, coordination chemistry, and usefulness in catalytic chemistry and organometallic synthesis in future studies.

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References

1. Darensbourg, D. G., Ortiz, C. G., & Kamplain, J. W. (2004). A New Water-Soluble Phosphine Derived from 1,3,5-Triaza-7-phosphaadamantane (PTA), 3,7-Diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane. Structural, Bonding, and Solubility Properties. *Organometallics*, 23 (8):1747-1754.
2. Elena Vergara, E., Miranda, S., Mohr, F., Cerrada, E., Tiekink, E. R. T., Romero, P., Mendía, A., & Laguna, M. (2007). Gold(I) and Palladium(II) Thiolato Complexes Containing Water-Soluble Phosphane Ligands. *European Journal of Inorganic Chemistry*, 18:2926-2933.
3. (a) Krogstad, D. A., Ellis, G. S., Gunderson, A. K., Hammirich, A. J., Rudolf, J. W., & Halfen, J. A. (2007). Two New Water-Soluble Derivatives of 1,3,5-Triaza-7-phosphaadamantane (PTA): Synthesis, Characterization, X-ray Analysis and Solubility Studies. *Polyhedron*, 26 (15):4093-4100.
(b) Gonsalvi, L., Guerriero, A., Hapiot, F., Krogstad, D. A., Monflier, E., Reginato, G. & Peruzzini, M. (2013). Lower- and Upper-Rim-Modified Derivatives of 1,3,5-Triaza-7-phosphaadamantane: Coordination Chemistry and Applications in Catalytic Reactions in Water. *Pure and Applied Chemistry*, 85 (2):385–396.
4. Tolman, C. A. (1977). Steric Effects of Phosphorus Ligands in Organometallic Chemistry and Homogeneous Catalysis. *Chemical Reviews*, 77 (3):313-348.



5. Mena-Cruz, A., Pablo, L., Romerosa, A., Saoud, M. & Serrano-Ruiz, M. (2007). Synthesis of the Water Soluble Ligands dmPTA and dmoPTA and the Complex $[\text{RuClCp}(\text{HdmPTA})(\text{PPh}_3)](\text{OSO}_2\text{CF}_3)$. *Inorganic Chemistry*, 46 (15):6120-6128.
6. Frost, B. J., Bautista, C. M., Huang, R., & Shearer, J. (2006). Manganese Complexes of 1,3,5-Triaza-7-phosphaadamantane (PTA): The First Nitrogen-Bound Transition-Metal Complex of PTA. *Inorganic Chemistry*, 45 (9):3481-3483.
7. Mohr, F., Falvello, L. R., & Laguna, M. (2006). A Silver(I) Coordination Polymer Containing Tridentate N- and P-Coordinating 1,3,5-Triaza-7-phosphaadamantane (PTA) Ligands. *European Journal of Inorganic Chemistry*, 16:3152-3154.
8. Bruker Analytical X-Ray, Madison, WI, USA (2010).
9. Sheldrick, G. M. (1996). SADABS, Program for Empirical Absorption Correction of Area Detector Data. University of Göttingen: Göttingen, Germany.
10. Sheldrick, G. M. (1998). SHELXS-97, Program for Crystal Structure Solution and Refinement. Institut Für Anorganische Chemie: Göttingen, Germany.
11. Sheldrick, G.M. (2008). A Short History of SHELX. *Acta Crystallographica*, A64:112-122.
12. Quin, L. D. (2000). *A Guide to Organophosphorus Chemistry*. New York: Wiley-Interscience, 1st Ed., 185-186.
13. Acharya, S. (2012). Synthesis and Catalytic Applications of Platinum(II) and Palladium(II)-PTA and DAPTA Complexes. University of Missouri- Saint Louis, Dissertations, 345:216.
14. Smoleńsky, P., Benisvy, L., Fátima, M., da Silva, C. G., & Pombeiro, A. J. L. (2009). Syntheses and Crystal Structures of the First Zinc Complex with 1,3,5-Triaza-7-phosphaadamantane (PTA), $[\text{ZnCl}_2(\text{PTA})_2]$, and of the Hybrid Organic-Inorganic Salts of N-Methyl-1,3,5-triaza-7-phosphaadamantane with Tetrahalozinc $[\text{PTA-Me}]_2-[\text{ZnI}_2\text{X}_2]$ (X = I, Cl). *European Journal of Inorganic Chemistry*, 9:1181-1186.
15. Darensbourg, D. J., Yarbrough, J. C., & Lewis, S. J. (2003). 2-Thia-1,3,5-triaza-7-phosphaadamantane 2,2-Dioxide (PASO₂). Comparative Structural and Reactivity Investigation with the Water-Soluble Phosphine Ligand 1,3,5-Triaza-7-phosphaadamantane (PTA). *Organometallics*, 22 (10):2050-2056.
16. Cederstam, A. K. & Novak, B. M. (1994). Investigations into the Chemistry of Thermodynamically Unstable Species. The Direct Polymerization of Vinyl Alcohol, the Enolic Tautomer of Acetaldehyde. *Journal of the American Chemical Society*, 116 (9):4073-4074.
17. Dubois, J. E., El-Alaoui, M. & Toullec, J. (1981). Kinetics and Thermodynamics of Keto-Enol Tautomerism of Simple Carbonyl Compounds: An Approach Based on a Kinetic Study of Halogenation at Low Halogen Concentrations. *Journal of the American Chemical Society*, 103 (18):5393-5401.

