1-Oxo-2,8-diaryl-2,5,8-triaza-1λ^5-phosphabicyclo[3.3.0]octanes as Substrates for the Preparation of Bis(2-arylaminoethyl)amines

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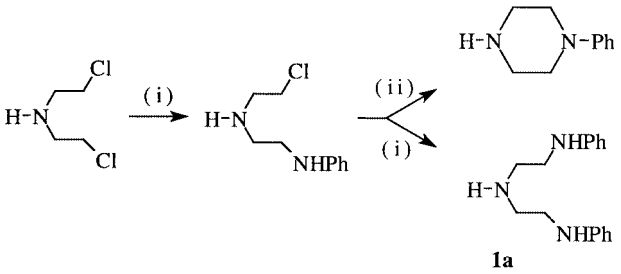
Abstract: A series of bis(2-arylaminoethyl)amines was prepared by hydrolysis of the corresponding bicyclic phosphoric triamides, followed in some cases by further functionalization.

Key words: diethylenetriamines, phosphoric triamides, hydrolysis of P-N bond

Ammonia and amines represent one of the most common types of F-donors ligands in coordination chemistry, and the polyamines with the typically 1,2- or 1,3-location of the amino groups are widely used as polydentate chelating ligand structures.[1] Bis-(2-aminoethyl)amine and its derivatives can coordinate a metal via two five membered chelate rings and should, according to their steric requirements,[2] show selectivity towards fairly large metal ions. The complexation of Cu^{2+} with 3,6,9-triazaundecane and its 1,11-disubstituted derivatives has been studied by potentiometric and spectrophotometric titrations.[3] The terdentate ligand derived from 3,9-diethyl-3,6,9-triazaundecane was used in a study of complexes of metals of the Ti and V triads.[4]

The obvious way to ethyleneamines and higher polyamines is to react ethylene dihalide with ammonia or with amines. The reaction was studied in late 1860's by Hofmann,[5] and the complexity of the reaction and its product was soon acknowledged. The reaction was reinvestigated by Mann,[6] who demonstrated that the parent triamine, bis(2-aminoethyl)amine ("diethylenetriamine") can be obtained in pure state as a hydrochloric acid salt only indirectly, via the Gabriel's method. The *N*,*N*′-diaryl substituted "diethylenetriamine", Ar-NH-CH_2CH_2- NH-CH_2CH_2-NH-Ar **1**, is an interesting example of that parent system because of the possibility of wide variations of its electronic and steric effects that may be achieved by introducing substituents to the aromatic groups, as well as at the nitrogen atoms of the 1,4,7-triazaheptane skeleton. The *N*,*N*′-diphenyl derivative **1a** (Ar = Ph), although a simple compound, is difficult to prepare. The patent literature reports formation of small quantities of **1a**, together with other amines, in the reduction of the nitrile of *N*-phenylglycine; the mixture of amines can be used as a vulcanization accelerator, antioxidant, or as an insect poison.[7] Compound **1a** is also formed as a side product (35%) together with *N*-phenylethylenediamine (65%) in the reaction of *N*-(2-chloroethyl)aniline with liquid NH_3.[8] Prelog and Driza have demonstrated long ago[9] that the reaction between bis(2-chloroethyl)amine and aniline is not a practical route to **1a**, since the major product of the reaction is *N*-phenylpiperazine (Scheme 1). We have repeated Prelog's experiment by reacting bis(2-chloroethyl)ammonium chloride with 5.1 mol equivalents of aniline in boiling toluene, and analyzsing the reaction product by high-resolution ^{1}H NMR spectroscopy. After neutralization, the reaction mixture consisted of *N*-phenylpiperazine, some **1a**, and aniline; the integration of the ^{1}H NMR signals indicated the preference for the intermediate monosubstitution product (Scheme 1) to undergo intramolecular cyclization (piperazine formation) rather than the second substitution (formation of **1a**) in a ratio of approximately 7:1.



1a

(i) $PhNH_2$

(ii) - HCl

Scheme 1

In this paper, we report an efficient and general method for the preparation of the triamines **1** from the corresponding bicyclic phosphoric triamides **2** (Scheme 2).

Substrates **2** have been first prepared in our laboratory,[10] (Scheme 3) and their structure and chemistry are being extensively studied.[11] Individual P-N bonds in **2** can be cleaved selectively,[11] but the exhaustive acid catalyzed hydrolysis of the P-N bonds, known to be a facile process,[12] seemed an obvious way to products **1**. The triamines **1** were isolated in the form of their trihydrochloride salts (highly insoluble, crystalline materials, easy to isolate and purify), and/or as free bases, and they were identified by NMR (^{1}H, ^{13}C) spectroscopy, MS, elemental analysis, and by conversion to the tri-*N*-acetyl derivatives. The latter compounds, unlike simple acetanilides, are rather low-melting solids or oils, and their ^{1}H NMR spectra show more than the expected number of signals of the *N*-acetyl methyl groups, as well as of other

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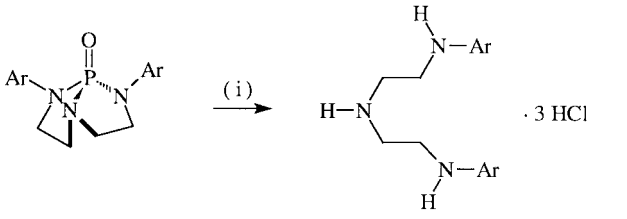


2 **1 · 3 HCl**

(i) aqueous - dioxane solution of HCl

1	Ar
a	C_6H_5
b	4-$CH_3C_6H_4$
c	4-$CH_3OC_6H_4$
d	4-BrC_6H_4
e	4-NCC_6H_4
f	4-$O_2NC_6H_4$

Scheme 2

groups in the molecule. It seems that the restricted rotation about the terminal amide bonds makes the tri-*N*-acetyl **1** to exist as a mixture of the possible *E*/*E*, *E*/*Z*, and *Z*/*Z* stereoisomers.

In the case of weakly nucleophilic anilines, some experimental problems were encountered. With *p*-bromoaniline, although the bicyclic amide **2d** was prepared in pure state and was hydrolyzed to **1d**, the formation of the intermediate noncyclic triamide (step (ii), Scheme 3) proceeded with very low yields. For the *p*-aminobenzonitrile, step (ii) did not present problems, but the last cyclization leading to **2e** required drastic conditions and **2e** was found to be rather unstable. It was therefore more convenient not to isolate **2e**, but to convert it in situ to the triamine **1e**. For the *p*-nitroaniline, we were not able to complete step (ii) because only the substitution of the first (*p*-nitrophenyl)amino group at the phosphoryl center proceeded with satisfactory rate. The triamine **1f** was however successfully prepared by the nitration of the tri-*N*-acetylated **1a** under conditions of highly selective para orientation, followed by the hydrolytical removal of the *N*-acetyl groups. The prepared products **1** and their derivatives are listed in the Table.

NMR spectra were recorded from $CDCl_3$ solutions on a Bruker AC 300 spectrometer. Mass spectra were recorded on a Varian MAT-212 double focusing direct inlet spectrometer at an ionization potential of 70 eV. IR spectra were recorded from CCl_4 solutions on a Bomem Michelson 100 spectrophotometer. Mps are uncorrected. Elemental analysis was performed at the department of Chemistry, University of Cape Town.

Substrates 2

Bicyclic phosphoric triamides **2a** (**2**, Ar = C_6H_5) and **2c** (**2**, Ar = C_6H_4-*p*-OMe) were prepared as described before.[10]

1-Oxo-2,8-di(4-methylphenyl)-2,5,8-triaza-1λ^5-phoshabicyclo-[3.3.0]octane (2b) (Ar = C_6H_4-*p*-Me)

The synthesis was carried out as described for **2a**,[10] using *N*-bis(2-chloroethyl)-N′,N″-di(4-methylphenyl)phosphotriamidate (4.89 g, 12.2 mmol) [prepared from *N*-bis(2-chloroethyl)phosphoramidodichloridate and *p*-toluidine; 76%; mp 124−129 °C, ^{31}P NMR: δ = 5.3], NaH (1.20 g, 48.8 mmol), and tetrabutylammonium bromide (TBAB) (0.194 g, 2.4 mmol) in anhyd THF (20 mL) without isolation of the monocyclic intermediate (see Scheme 3). The product was purified by dissolving it in a minimum volume of $CHCl_3$ and precipitating with a large volume of cold hexane.

Yield = 3.60 g (90%), mp 186−187 °C.

^{31}P NMR: δ = 33.7.

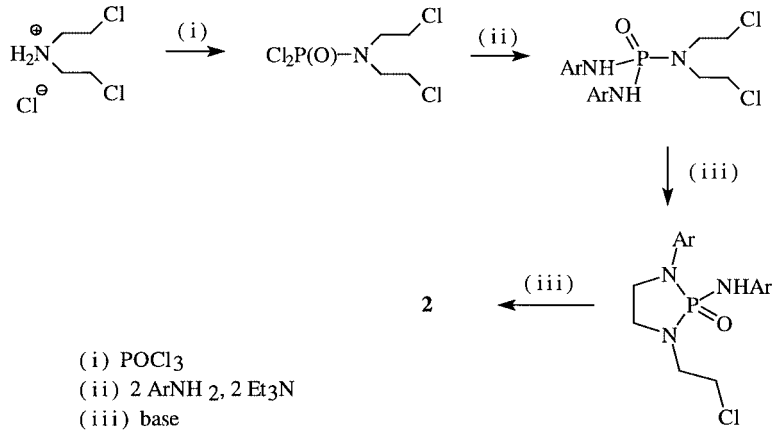
^{1}H NMR: δ = 2.40 (s, 6H, 2 C*H*$_3$), 3.09−3.21 (m, 2H, 2 NC*H*), 3.59−3.80 (m, 4H, 4 NC*H*), 3.84−3.94 (m, 2H, 2 NC*H*), 7.00 (d, 4H, J_{HH} = 8.5 Hz, 4 *m*-*H*$_{arom}$), 7.06 (d, 4H, J_{HH} = 8.5 Hz, 4 *o*-*H*$_{arom}$).

^{13}C NMR: δ = 21.0 (s, *C*H$_3$), 48.3 (d, J_{CP} = 7.1 Hz, NCH$_2$), 49.4 (d, J_{CP} = 19.8 Hz, NCH$_2$), 119.4 (s, *C*$_{arom}$), 129.9 (s, *C*$_{arom}$), 132.0 (s, *C*$_{arom}$), 139.8 (s, *C*$_{arom}$).

Anal. Calcd for $C_{18}H_{22}N_3OP$: C, 66.04; H, 6.77; N, 12.84. Found: C, 65.88; H, 6.90; N, 12.49.

1-Oxo-2,8-di(4-bromophenyl)-2,5,8-triaza-1λ^5-phosphabicyclo-[3.3.0]octane (2d) (Ar = C_6H_4-*p*-Br)

Prepared by converting *N*-bis(2-chloroethyl)phosphoramidodichloridate (5.0 g, 19 mmol) with 4-bromoaniline (3.27 g, 19 mmol) in CH_2Cl_2 (90mL) in the presence of the excess of Et_3N into the corre-



Scheme 3

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Table Triamines 4-X$C_6H_4NHCH_2CH_2NHCH_2CH_2NHC_6H_4$-4-X **1** and their Derivatives

Compound	X	Preparation	Data for **1** Yield; ^{1}H, ^{13}C NMR ($CDCl_3$), δ, *J* (Hz)	Derivatives Mp; ^{1}H, ^{13}C NMR ($CDCl_3$), δ, *J* (Hz)
1a	H	Hydrolysis of **2a** (0.84 g, 2.8 mmol)	Yield: 0.72 g (100%); oil. ^{1}H NMR: 2.88 (t, 4 H, J_{HH} = 5.7, 2 NCH_2), 3.21 (t, 4 H, J_{HH} = 5.7, 2 ArNCH_2), 4.01 (br s, 3 H, 3 N*H*), 6.63 (d, 4 H, J_{HH} = 8.0, 4 *o*-H_{arom}), 6.71 (t, 2 H, J_{HH} = 7.5, 2 *p*-H_{arom}), 7.18 (dd, 4 H, J_{HH} = 8.0, 7.5, 4 *m*-H_{arom}); ^{13}C NMR: 44.3 (s, N*C*H$_2$), 49.1 (s, ArN*C*H$_2$), 113.6 (s, *o*-C_{arom}), 118.1 (s, *p*-C_{arom}), 129.9 (s, *m*-C_{arom}), 149.0 (s, *ipso*-C_{arom})	*Trihydrochloride*. Mp 203−206 °C. ^{1}H NMR (MeOD): 3.28 t, 4 H, J_{HH} = 5.9, 2 NCH_2), 3.49 (t, 4 H, J_{HH} = 6.0, 2 ArNCH_2), 6.67−6.71 (m, 6 H, 4 *o*-H_{arom}, 2 *p*-H_{arom}), 7.15 (t, 4 H, J_{HH} = 6.0, 4 *m*-H_{arom}); ^{13}C NMR: 41.1 (s, N*C*H$_2$), 48.1 (s, ArN*C*H$_2$), 114.3 (s, *o*-C_{arom}), 119.1 (s, *p*-C_{arom}), 130.3 (s, *m*-C_{arom}), 149.1 (s, *ipso*-C_{arom}). *N,N',N"-triacetyl* (63%). Mp 111−113°C ($CHCl_3$/pet. ether, 2:1). ^{1}H NMR: 1.78 (s, 3H, NAc), 1.85 (s, 3H, NAc), 2.03 (s, 3 H, NAc), 3.43 (t, 2 H, J_{HH} = 6.5, N*C*H$_2$), 3.61 (t, 2 H, J_{HH} = 7.1, NCH_2), 3.76 (t, 2 H, J_{HH} = 6.5, ArNCH_2), 3.80 (t, 2 H, J_{HH} = 7.2, ArNCH_2), 7.16 (d, 2 H, J_{HH} = 7.2, 2 *o*-H_{arom}), 7.20 (d, 2 H, J_{HH} = 7.0, 2 *o*-H_{arom}), 7.28−7.47 (m, 6 H, 2 *p*-H_{arom}, 4 *m*-H_{arom}); ^{13}C NMR: 21.9 (s, *C*H$_3$ of Ac), 23.2 (s, *C*H$_3$ of Ac), 44.0, 46.8, 47,4, 48.8 (s, N*C*H$_2$), 128.1, 128.3 (s, *o*-C_{arom}), 128.4, 128.8 (s, *p*-C_{arom}), 130.3, 130.6 (s, *m*-C_{arom}), 143.87, 143.93 (s, *ipso*-C_{arom}), 171.3, 171.4, 171.8 (s, *C*=O)[a]
1b	CH_3	Hydrolysis of **2b** (2.00 g, 6.11 mmol)	Yield: 1.15 g (67%); oil. ^{1}H NMR: 2.25 (s, 6 H, 2 ArCH_3), 2.89 (t, 4 H, J_{HH} = 5.8, 4 NCH_2), 3.21 (t, 4 H, J_{HH} = 5.8, 4 ArNCH_2), 3.71 (s, 3 H, 3 N*H*), 6.56 (d, 4 H, J_{HH} = 8.3, 4 *o*-H_{arom}), 6.99 (d, 4 H, J_{HH} = 8.0, 4 *m*-H_{arom}); ^{13}C NMR: 21.0 (s, Ar*C*H$_3$), 44.7 (s, N*C*H$_2$), 49.2 (s, ArN*C*H$_2$), 113.8 (s, *o*-C_{arom}), 127.4 (s, *p*-C_{arom}), 130.4 (s, *m*-C_{arom}), 146.8 (s, *ipso*-C_{arom})[b]	*N,N',N"-triacetyl* (81%). Purified by column chromatography (SiO_2, acetone/$CHCl_3$, 1:1); oil. ^{1}H NMR: 1.71 (s, 3 H, ArCH_3), 1.77 (s, 3 H, ArCH_3), 1.97 (s, 3 H, NAc), 2.28 (s, 3 H, NAc), 2.31 (s, 3 H, NAc), 3.36 (t, 2 H, J_{HH} = 6.1, 2 NCH_2), 3.53 (t, 2 H, J_{HH} = 7.0, 2 NCH_2), 3.65−3.73 (m, 4 H, 4 ArNCH_2), 6.98 (d, 2 H, J_{HH} = 8.0, 2 *o*-H_{arom}), 7.02 (d, 2 H, J_{HH} = 8.3, 2 *o*-H_{arom}), 7.10 (d, 2 H, J_{HH} = 8.0, 2 *m*-H_{arom}), 7.14 (d, 2 H, J_{HH} = 8.2, 2 *m*-H_{arom}); ^{13}C NMR: 21.5 (s, Ar*C*H$_3$), 21.8 (s, *C*H$_3$ of NAc), 23.0 (s, *C*H$_3$ of NAc), 43.8, 46.7, 47.3, 48.7 (s, N*C*H$_2$), 127.8, 127.9 (s, *o*-C_{arom}), 130.8, 131.1 (s, *m*-C_{arom}), 138.2, 138.6 (s, *p*-C_{arom}), 141.2, 141.3 (s, *ipso*-C_{arom}), 171.4, 171.5, 171,7 (s, *C*=O)[c]
1c	OCH_3	Hydrolysis of **2c** (0.30 g, 0.83 mmol)	Yield: 0.25 g (95%); oil. ^{1}H NMR: 2.88 (t, 4 H, J_{HH} = 5.7, 2 NCH_2), 3.18 (t, 4 H, J_{HH} = 5.8, 2 ArNCH_2), 3.70 (br s, 3 H, 3 N*H*), 3.75 (s, 6 H, 2 OCH_3), 6.60 (d, 4 H, J_{HH} = 8.8, 4 *m*-H_{arom}), 6.78 (d, 4 H, J_{HH} = 9.0, 4 *o*-H_{arom}); ^{13}C NMR: 45.4 (s, N*C*H$_2$), 49.3 (s, ArN*C*H$_2$), 56.5 (s, O*C*H$_3$), 115.0 (s, *m*-C_{arom}), 115.6 (s, *o*-C_{arom}), 143.4 (s, *ipso*-C_{arom}), 152.9 (s, *p*-C_{arom})	*Trihydrochloride*. Mp 207−209.5 °C. ^{1}H NMR (CD_3OD): 3.49 (t, 4 H, J_{HH} = 6.3, 2 NCH_2), 3.73 (t, 4 H, J_{HH} = 6.2, 2 ArNCH_2), 3.96 (s, 6H, 2OCH_3), 7.04 (d, 4 H, J_{HH} = 8.8, 4 *m*-H_{arom}), 7.36 (d, 4 H, J_{HH} = 8.8, 4 *o*-H_{arom}); ^{13}C NMR: 45.3 (s, N*C*H$_2$), 47.2 (s, ArN*C*H$_2$), 56.3 (s, O*C*H$_3$), 116.6 (s, *m*-C_{arom}), 123.3 (s, *o*-C_{arom}), 125.2 (s, *ipso*-C_{arom}), 160.7 (s, *p*-C_{arom})[d] *N,N',N"-triacetyl* (90%). Oil.^{1}H NMR: 1.68 (s, 3H, NAc), 1.74 (s, 3 H, NAc), 1.95 (s, 3 H, NAc), 3.35 (t, 2 H, J_{HH} = 6.1, 2 NCH_2), 3.51 (t, 2 H, J_{HH} = 6.9, 2 NCH_2), 3.62−3.67 (m, 4 H, 4 ArNCH_2), 3.71 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 6.80 (d, 2 H, J_{HH} = 8.5, 2 *m*-H_{arom}), 6.84 (d, 2 H, J_{HH} = 8.8, 2 *m*-H_{arom}), 6.99 (d, 2 H, J_{HH} = 8.8, 2 *o*-H_{arom}), 7.01 (d, 2 H, J_{HH} = 8.8, 2 *o*-H_{arom}); ^{13}C NMR: 21.7 (s, *C*H$_3$ of NAc), 22.9 (s, *C*H$_3$ of NAc), 43.7, 46.5, 47.3, 48.6 (s, 4 N*C*H$_2$), 55.88 (s, O*C*H$_3$), 55.92 (s, O*C*H$_3$), 115.2, 115.6 (s, 2 *m*-C_{arom}), 129.1, 129.2 (s, 2 *o*-C_{arom}), 136.4, 136.5 (s, 2 *ipso*-C_{arom}), 159.4, 159.6 (s, 2 *p*-C_{arom}), 171.75 (s, *C*=O), 171.84 (s, *C*=O)
1d	Br	Hydrolysis of **2d** (0.10 g, 0.22 mmol)	Yield: 0.075 g (83%); mp 60−61.5 °C. ^{1}H NMR: 2.97 (t, 4 H, J_{HH} = 5.7, 4 NCH_2), 3.27 (t, 4 H, J_{HH} = 5.5, 4 ArNCH_2), 4.15 (br s, 3 H, 3 N*H*), 6.58 (d, 4 H, J_{HH} = 8.8, 4 *o*-H_{arom}), 7.33 (d, 4 H, J_{HH} = 8.5, 4 *m*-H_{arom}); ^{13}C NMR: 44.3 (s, N*C*H$_2$), 49.0 (s, ArN*C*H$_2$), 109.8 (s, *ipso*-C_{arom}), 115.2 (s, *o*-C_{arom}), 132.6 (s, *m*-C_{arom}), 148.0 (s, *p*-C_{arom})	Trihydrochloride. Mp 214–216 °C. ^{1}H NMR (CD_3OD): 3.26 (t, 4 H, J_{HH} = 5.9, 4 NCH$_2$), 3.46 (t, 4 H, J_{HH} = 5.9, 4 ArNCH$_2$), 6.62 (d, 4 H, J_{HH} = 8.5, 4 o-H_{arom}), 7.23 (d, 4 H, J_{HH} = 8.8, 4 m-H_{arom}); ^{13}C NMR: 41.1 (s, NCH$_2$), 47.8 (s, ArNCH$_2$), 110.8 (s, ipso-C_{arom}), 116.1 (s, o-C_{arom}), 133.0 (s, m-C_{arom}), 148.0 (s, p-C_{arom})[e]

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Table (continued)

Compound	X	Preparation	Data for **1** Yield; ^{1}H, ^{13}C NMR ($CDCl_3$), δ, *J* (Hz)	Derivatives Mp; ^{1}H, ^{13}C NMR ($CDCl_3$), δ, *J* (Hz)
1e	CN	Neutralisation of the trihydrochloride salt, prepared by hydrolysis of the corresponding 1,3,2-diazaphospholidine (see Discussion)	Yield: 0.050 g (82%); mp 118 °C. ^{1}H NMR: 2.93 (t, 4 H, J_{HH} = 5.7, 4 NCH_2), 3.26 (t, 4 H, J_{HH} = 5.4, 4 ArNCH_2), 4.61 (br s, 3 H, 3 N*H*), 6.56 (d, 4 H, J_{HH} = 8.3, 4 *o*-H_{arom}), 7.42 (d, 4 H, J_{HH} = 8.5, 4 *m*-H_{arom}); ^{13}C NMR: 43.4 (s, NCH_2), 48.6 (s, ArNCH_2), 99.8 (s, *ipso*-C_{arom}), 113.0 (s, *o*-C_{arom}), 121.0 (s, *C*N), 134.5 (s, *m*-C_{arom}), 152.0 (s, *p*-C_{arom})	Trihydrochloride. Mp 211–212 °C ^{1}H NMR (CD_3OD): 3.30 (t, 4 H, J_{HH} = 6.1, 4 NCH_2), 3.58 (t, 4 H, J_{HH} = 6.1, 4 $ArNCH_2$), 6.76 (d, 4 H, J_{HH} = 8.5, 4 o-H_{arom}), 7.46 (d, 4 H, J_{HH} = 8.8, 4 m-H_{arom}); ^{13}C NMR: 40.2 (s, NCH_2), 47.7 (s $ArNCH_2$), 99.8 (s, ipso-C_{arom}), 113.8 (s, o-C_{arom}), 121.2 (s, CN), 134.8 (s, m-C_{arom}), 152.9 (s, p-C_{arom}); IR: ν_{CN} = 2213.8 cm^{-1} [f]
1f	NO_2	From triacetyl derivative of **1a**, via nitration followed by hydrolysis (0.20 g, 0.42 mmol)	Yield: 0.083 g (57%). Yellow powder, mp 145–147.5 °C. ^{1}H NMR: 2.97 (t, 4 H, J_{HH} = 5.7, 4 NCH_2), 3.32 (t, 4 H, J_{HH} = 4.8 Hz, ArNCH_2), 4.89 (br s, 3H, 3 N*H*), 6.54 (d, 4 H, J_{HH} = 9.3, 4 *o*-H_{arom}), 8.09 (d, 4 H, J_{HH} = 9.3, 4 *m*-H_{arom}); ^{13}C NMR: 43.6 (s, NCH_2), 48.6 (s, ArNCH_2), 111.9 (s, *o*-C_{arom}), 127.1 (s, *m*-C_{arom}), 139.1 (s, *ipso*-C_{arom}), 153.9 (s, *p*-C_{arom})[g]	*N,N′,N″-triacetyl*. (100%). Yellow powder, mp 99–102 °C. ^{1}H NMR:1.87 (s, 3 H, NAc), 1.94 (s, 3 H, NAc), 2.05 (s, 3 H, NAc), 3.43 (t, 2 H, J_{HH} = 6.5, 2 NCH_2), 3.63 (t, 2 H, J_{HH} = 7.2, 2 NCH_2), 3.79 (t, 2 H, J_{HH} = 6.3, 2 ArNCH_2), 3.87 (t, 2 H, J_{HH} = 7.2, 2 ArNCH_2), 7.40 (d, 2 H, J_{HH} = 9.0, 2 *o*-H_{arom}), 7.44 (d, 2 H, J_{HH} = 9.0, 2 *o*-H_{arom}), 8.28 (d, 2 H, J_{HH} = 9.0, 2 *m*-H_{arom}), 8.32 (d, 2 H, J_{HH} = 8.8, 2 *m*-H_{arom}); ^{13}C NMR: 22.0 (s, *C*H_3 of NAc), 23.4 (s, *C*H_3 of NAc), 44.1, 46.9, 47.8, 49.2 (s, 4 NCH_2), 125.9, 126.2 (s, *o*-C_{arom}), 129.0, 129.2 (s, *m*-C_{arom}), 128.2, 130.8 (s, *ipso*-C_{arom}), 147.5, 149.5 (s, *p*-C_{arom}), 170.8, 172.0 (s, *C*=O); IR: ν_{NO2} = 1521.8 cm^{-1}

[a] Anal. Calcd ($C_{22}H_{27}N_3O_3$): C, 69.27; H, 7.13; N, 11.01. Found: C, 69.50; H, 7.31; N, 10.86.
[b] Anal. Calcd ($C_{18}H_{25}N_3$): C, 76.28; H, 8.89; N, 14.83. Found: C, 76.10; H, 9.00; N, 14.65.
[c] Anal. Calcd ($C_{24}H_{31}N_3O_3$): C, 70.39; H, 7.63; N, 10.26. Found: C, 70.15; H, 7.80; N, 10.14.
[d] Anal. Calcd ($C_{18}H_{28}Cl_3N_3O_2$): C, 50.89; H, 6.64; N, 9.89. Found: C, 50.61; H, 6.99; N, 9.35.
[e] Anal. Calcd ($C_{16}H_{22}Br_2Cl_3N_3$): C, 36.78; H, 4.24; N, 8.04. Found: C, 36.48; H, 4.38; N, 7.91.
[f] Anal. Calcd ($C_{18}H_{22}Cl_3N_5$): C, 52.13; H, 5.35; N, 16.88. Found: C, 51.85; H, 5.50; N, 16.42.
[g] Anal. Calcd ($C_{16}H_{19}N_5O_4$): C, 55.65; H, 5.54; N, 20.28. Found: C, 55.40; H, 5.61; N, 19.89).

sponding 3-(2-chloroethyl)-2-oxo-1-(4-bromophenyl)-1-(4-bromophenyl)amino-1,3,2-diazaphospholidine (0.55 g, 6%; mp 221–222.5 °C; ^{31}P NMR: δ = 13.5, ^{1}H and ^{13}C NMR and mass spectra in full agreement with the expected structure), which was then converted to **2d** with NaH (1.5 mol-equiv.) in THF (20 mL) at r.t.

Yield = 0.22 g (79%), mp 203–204 °C ($CHCl_3$/hexane, 1:1).

^{31}P NMR: δ = 32.9.

^{1}H NMR: δ = 3.12–3.24 (m, 2H, 2 NC*H*), 3.56–3.67 (m, 2H, 2 NC*H*), 3.73–3.93 (m, 4H, 4 NC*H*), 7.06 (d, 4H, J_{HH} = 9.0 Hz, 4 *o*-H_{arom}), 7.30 (d, 4H, J_{HH} = 8.8 Hz, 4 *m*-H_{arom}).

^{13}C NMR: δ = 48.6 (d, J_{CP} = 7.2 Hz, NCH_2), 49.9 (d, J_{CP} = 19.8 Hz, ArNCH_2), 115.8 (s, *ipso*-C_{arom}), 121.1 (d, J_{CP} = 3.6 Hz, *o*-C_{arom}), 132.6 (s, *m*-C_{arom}), 141.6 (s, *p*-C_{arom}).

MS: *m/z* 458, 457, 456 (77, 99, 100 %, M^+).

Anal. Calcd for $C_{16}H_{16}Br_2N_3OP$: C, 42.02; H, 3.53; N, 9.19. Found: C, 41.98; H, 3.65; N, 9.05.

1-Oxo-2,8-di(4-cyanophenyl)-2,5,8-triaza-1λ^5-phosphabicyclo-[3.3.0]octane (2e) (Ar = C_6H_4-*p*-CN):
Synthesized by initial preparation of 3-(2-chloroethyl)-2-oxo-1-(4-cyanophenyl)-1-(4-cyanophenyl)amino-1,3,2-diazaphospholidine as described above (1.58 g, 19%; mp 233–234 °C; ^{31}P NMR: δ = 11.4. ^{1}H and ^{13}C NMR spectra and mass spectra in full agreement with the expected structure), which was then converted to **2e** with LDA (1.5 mol-equiv.) in refluxing toluene (20 mL).

Yield = 0.08 g (64%), mp 189–191 °C (acetone/hexane, 1:1).

^{31}P NMR: δ = 32.1.

^{1}H NMR: δ = 3.19–3.31 (m, 2H, 2 NC*H*), 3.61–3.75 (m, 2H, 2 NC*H*), 3.79–4.01 (m, 4H, 4 NC*H*), 7.30 (d, 4H, J_{HH} = 8.5 Hz, 4 *o*-H_{arom}), 7.49 (d, 4H, J_{HH} = 8.6 Hz, 4 *m*-H_{arom}).

^{13}C NMR: δ = 48.7 (d, J_{CP} = 7.2 Hz, NCH_2), 50.1 (d, J_{CP} = 19.7 Hz, ArNCH_2), 106.1 (s, *ipso*-C_{arom}), 119.0 (d, J_{CP} = 3.6 Hz, *o*-C_{arom}), 119.5 (s, *C*N), 134.0 (s, *m*-C_{arom}), 146.7 (s, *p*-C_{arom}).

Anal. Calcd for ($C_{18}H_{16}N_5OP$): C, 61.89; H, 4.62; N, 20.05. Found: C, 61.66; H, 4.70; N, 19.88.

Triamines 1 (Hydrolysis of Triamides 2); General Procedure
To a solution of **2** (approx 0.10 g) in 1,4-dioxane (10 mL) was added dropwise with stirring HCl (3–6 equiv, as a 10% aq solution, or as concd aq solution), and the solution was stirred at r.t. for 24 h. For **1a**, **1c**, **1d** the corresponding trihydrochloride salts precipitated out, and were isolated by cooling the mixture to 10 °C and filtration. For a direct isolation of free amines **1** most of dioxane and H_2O was removed under reduced pressure, NaOH (at least 6 equiv, as a 5% aqueous solution) was added to the residual paste (pH >9), and the mixture was stirred at r.t. for 1 h. The mixture was diluted twice with H_2O, extracted with $CHCl_3$, and the $CHCl_3$ solution was washed with H_2O until pH 8 was reached. After drying ($MgSO_4$) and evaporation of the solvent under reduced pressure, the product was kept under a vacuum of approx 10^{-2} mm Hg for 1 h.

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Acetylation of Triamines 1; General Procedure

A solution of amine **1** in acetic anhydride (approx 8 mL/g of **1**) was heated under reflux for 2 h and poured into cold water (approx 6 mL/mL of Ac_2O). The solution was extracted with $CHCl_3$ (approx 1 mL per 3 mL of H_2O used), the $CHCl_3$ solution was washed twice with equal volume of H_2O and once with half of the volume of 5% aq Na_2CO_3 (pH X8). After drying ($MgSO_4$) and evaporation of the solvent under reduced pressure, the triacetate was purified by crystallization.

Nitration of *N,N',N"*-Triacetyl 1a

Tri-*N*-acetyl derivative of **1a** (1.0 g, 2.62 mmol) was dissolved in glacial HOAc (6 mL) and concd H_2SO_4 (6 mL) was added with stirring. A mixture of HNO_3 (0.5 mL) and concd H_2SO_4 (0.4 mL) was added dropwise with stirring and cooling (inside temperature below 10 °C). The solution was allowed to warm to r.t. and stirred for further 48 h. Cold H_2O (50 mL) was added slowly with cooling the flask in ice; the precipitated yellow product was filtered off, washed with H_2O and dried. The product crystallized after keeping it in a refrigerator; yield 1.23 g (100%).

Hydrolysis of the Nitration Product (Preparation of 1f)

A suspension of the above product (0.20 g, 0.42 mmol) in 20% aq HCl (3 mL) was heated under reflux for 1 h. The hot mixture was poured into cold H_2O (20 mL) and neutralized with 10% aq NaOH with cooling. The mixture was kept in a refrigerator overnight and the precipitated product was filtered off and dried.

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