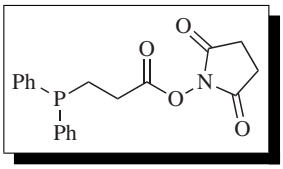
1-[3-(Diphenylphosphino)-propanoyl]-2, 5-pyrrolidindione



[170278-50-9] $C_{19}H_{18}NO_4P$ (MW 355.32)

InChI = 1S/C19H18NO4P/c21-17-11-12-18(22)20(17)24-19(23)13-14-25(15-7-3-1-4-8-15)16-9-5-2-6-10-16/h1-10H,11-14H2

InChIKey = QRRPSWGREIRROT-UHFFFAOYSA-N

(reagent for the conversion of azides into the corresponding diazo compounds[1])

Alternate Name: N-succinimidyl 3-(diphenylphosphino)propionate (DPPS).

Physical Data: mp 104–108 °C.

Solubility: soluble in most organic solvents.

Form Supplied in: white solid.

Analysis of Reagent Purity: >98% (HPLC).

Preparative Method: prepared by the coupling of 3-(diphenylphosphino)propionic acid and *N*-hydroxysuccinimide with DCC or DIC.[1–3]

Purification: purified over silica gel flash column chromatography eluting with 30% EtOAc in hexanes.

Original Commentary

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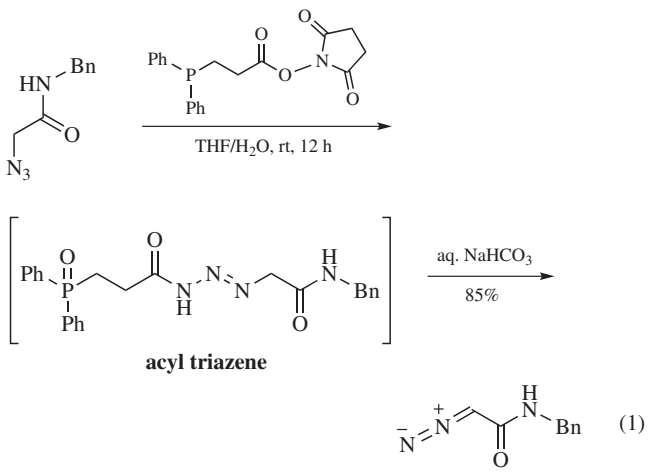
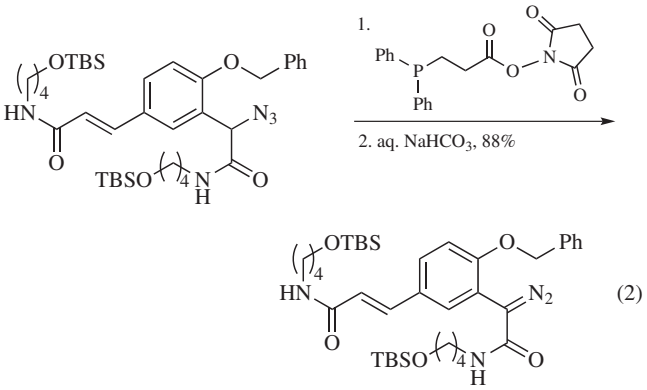
Azides to Diazo Compounds. Raines and Myers demonstrated the application of DPPS as an efficient phosphine reagent for the conversion of azides into the corresponding diazo compounds under very mild conditions. The reaction proceeds via an acyl triazene intermediate that converts to the corresponding diazo compound under mild basic conditions (eq 1). This "deimidogenation" reaction is highly selective and tolerates a wide range of functional groups.



(1)

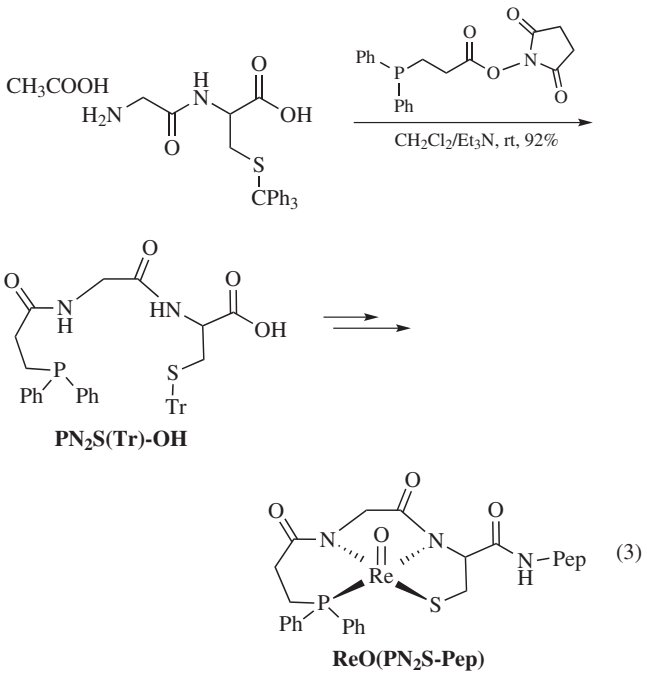
Wakimoto et al. applied this mild reagent to synthesize the key "diazoamide intermediate" during their total synthesis of aperidine. In this transformation, azide was first activated with DPPS to form an acyl triazene intermediate that was subsequently transformed by treatment with aqueous $NaHCO_3$ to the corresponding diazoamide (eq 2).[4]



(2)

This is noteworthy that other diazo transfer reagents such as *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) failed completely to afford the key diazoamide intermediate.[4]

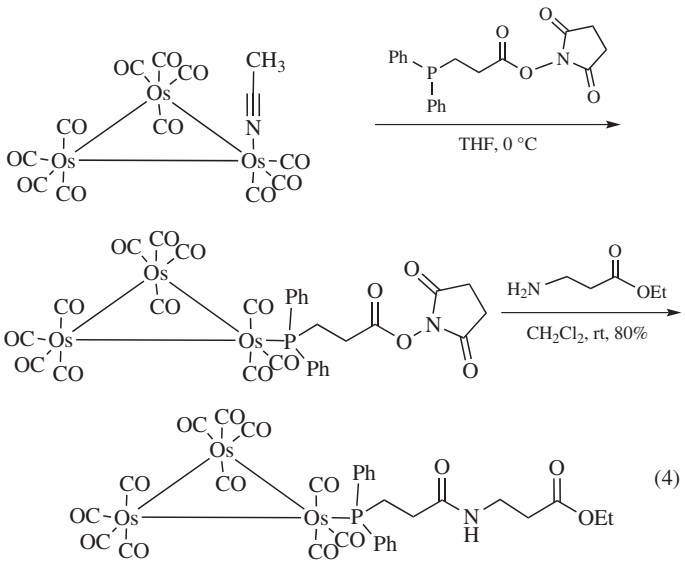
Application in Protein Labeling. DPPS was applied by Mazzi and coworkers for the synthesis of a PN_2S ligand to form stable rhenium(V) oxo complexes [$ReO(PN_2S$-Pep)] that are used for site-specific radiolabeling of proteins.[5–8] Glycyl-*S*-trityl-L-cysteine acetate was coupled with DPPS to synthesize $PN_2S(Tr)OH$ that was used to form stable Re(V) oxo complexes (eq 3).[8]



(3)

Osella et al. also used DPPS as a phosphine linker for protein labeling. The phosphine in DPPS acts as a ligand to coordinate with heavy-metal clusters, while the *N*-succinimidyl ester acts as a linker that acylates amine side chains for labeling of proteins (eq 4).[9] In a model reaction, $Os_3(CO)_{11}$DPPS reacted with a

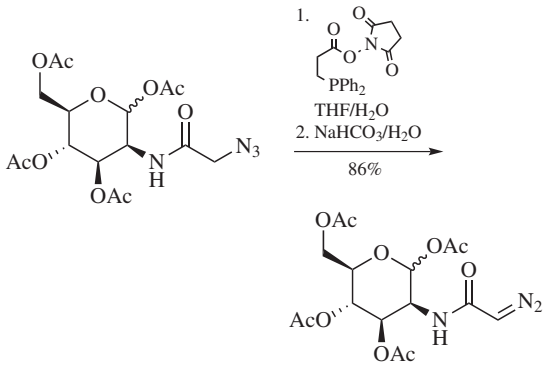
β-alanine ester to afford the desired amide in excellent yield (eq 4). In a similar manner, bovine serum albumin (BSA) was also labeled in the range of 20–30% yields with DPPS metal cluster linkers.



(4)

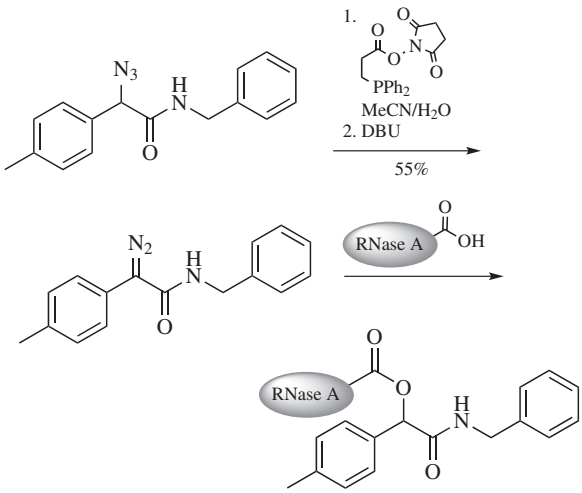
Miscellaneous. Recently, DPPS has also been used to incorporate phosphine moieties into the cyclic decapeptide gramicidin S via amide bond formation with the lysine side-chain amines. The phosphine-containing gramicidine S derivatives were used as novel ligands for asymmetric catalysis resulting in up to 52% ee in Rh-catalyzed asymmetric hydrogenation and up to 15% ee in Pd-catalyzed allylic substitution.[3]

Related Reagents. *N*-[2-(Diphenylphosphino)benzoyloxy]-succinimide; ethyl 2-diphenylphosphinobenzoate; 2-(Diphenylphosphino)terephthalic acid 1-methyl 4-pentafluorophenyl diester.



(5)

Mix and Raines used DPPS to generate diazo compounds that could label proteins by esterification. Through a Hammett analysis, a diazo-functionalized (*p*-methylphenyl)-glycinamide was identified as an optimal compound for the esterification of protein carboxyl groups (eq 6).[12]



(6)

First Update

Lindsey R. Orgren & Ronald T. Raines
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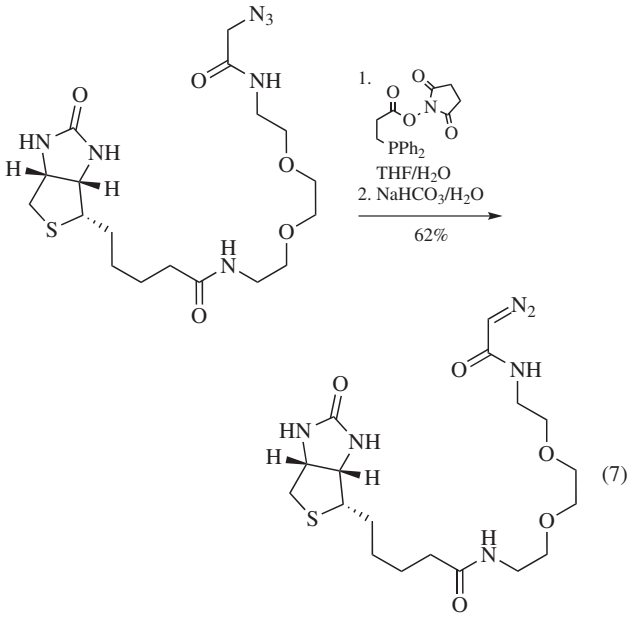
Azides to Diazo Compounds. Deimidogenation of azides with DPPS was used to produce a variety of diazo compounds, extending the scope of the seminal paper.[10]

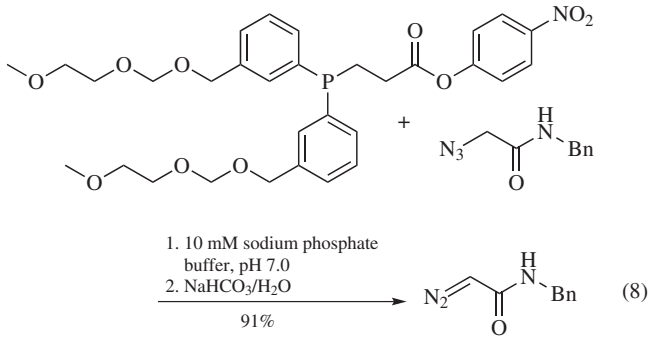
Andersen et al. established the biological stability of a diazo group by using DPPS to produce a diazo-functionalized *N*-acetylmannosamine (eq 5), which was found to endure cellular metabolism and label the surface of mammalian cells.[11]

Aronoff et al. investigated a means to establish chemoselective 1,3-dipolar cycloadditions of a diazo group generated from an azido group with DPPS. By tuning the electronics of the dipolarophile, cycloaddition with a diazo compound was obtained in the presence of the azide precursor. These workers also employed DPPS-mediated deimidogenation on an azidoacetamide–biotin conjugate to produce a diazoacetamide–biotin conjugate (eq 7) that undergoes cycloaddition with dehydroalanine residues on nisin, unlike the azidoacetamide–biotin precursor.[13]



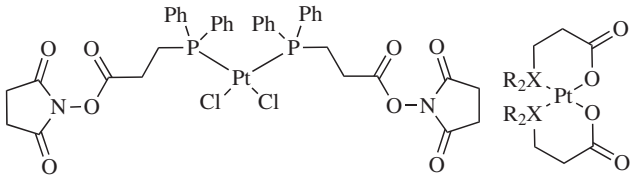
(7)

Chou and Raines developed a water-soluble analog of DPPS that is capable of performing the deimidogenation reaction in an aqueous environment and is tolerant of biological nucleophiles (eq 8). The chromogenic nature of this reagent also enables monitoring of reaction progress.[14]



(8)

Miscellaneous. Ravera et al. investigated the antiproliferative activity of cisplatin-like Pt(II)-phosphane complexes in tumor cell lines. DPPS was used as a ligand that would retain its "fully opened" form, incapable of undergoing an intramolecular rearrangement into the closed form, as did unprotected compounds (eq 9). Only the open form manifested antiproliferative activity.[15]



Fully open form

Fully closed form
X = P, N; R = Ph, H

(9)

1. Myers, E. L.; Raines, R. T., *Angew. Chem., Int. Ed.* **2009**, *48*, 2359.
2. Huang, L.; Wulff, W. D., *J. Am. Chem. Soc.* **2011**, *133*, 8892.
3. Guisado-Barrios, G.; Munoz, B. K.; Kamer, P. C. J.; Lastdrager, B.; van der Marel, G.; Overhand, M.; Vega-Vazquez, M.; Martin-Pastor, M., *Dalton Trans.* **2013**, *42*, 1973.
4. Wakimoto, T.; Miyata, K.; Ohuchi, H.; Asakawa, T.; Nukaya, H.; Suwa, Y.; Kan, T., *Org. Lett.* **2011**, *13*, 2789.
5. Santimaria, M.; Maina, T.; Mazzi, U.; Nicolini, M., *Inorg. Chim. Acta* **1995**, *240*, 291.
6. Santimaria, M.; Mazzi, U.; Gatto, S.; Dolmella, A.; Bandoli, G.; Nicolini, M., *J. Chem. Soc., Dalton Trans.* **1997**, 1765.
7. Morelli, G.; De, L. S.; Tesauro, D.; Saviano, M.; Pedone, C.; Dolmella, A.; Visentin, R.; Mazzi, U., *J. Pept. Sci.* **2002**, *8*, 373.
8. Visentin, R.; Rossin, R.; Giron, M. C.; Dolmella, A.; Bandoli, G.; Mazzi, U., *Inorg. Chem.* **2003**, *42*, 950.
9. Osella, D.; Pollone, P.; Ravera, M.; Salmain, M.; Jaouen, G., *Bioconjug. Chem.* **1999**, *10*, 607.
10. (a) Friscourt, F.; Fahrni, C. J.; Boons, G.-J., *Chem. Eur. J.* **2015**, *21*, 13996. (b) DeAngelis, A.; Dmitrenko, O.; Fox, J. M., *J. Am. Chem. Soc.* **2012**, *134*, 11035.
11. Andersen, K. A.; Aronoff, M. R.; McGrath, N. A.; Raines, R. T., *J. Am. Chem. Soc.* **2015**, *137*, 2412.
12. Mix, K. A.; Raines, R. T., *Org. Lett.* **2015**, *17*, 2358.
13. Aronoff, M. R.; Gold, B.; Raines, R. T., *Org. Lett.* **2016**, *18*, 1538.
14. Chou, H.-H.; Raines, R. T., *J. Am. Chem. Soc.*, **2013**, *135*, 14936.
15. Ravera, M.; Gabano, E.; Sardi. M.; Monti, E.; Gariboldi, M.; Osella, D., *Eur. J. Inorg. Chem.*, **2012**, 3441.