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Selective derivatization of 2,4,6-triazidopyridines by the Staudinger reaction

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The selective addition of triphenylphosphine to the -azido group of 2,4,6-triazidopyridines has been developed.

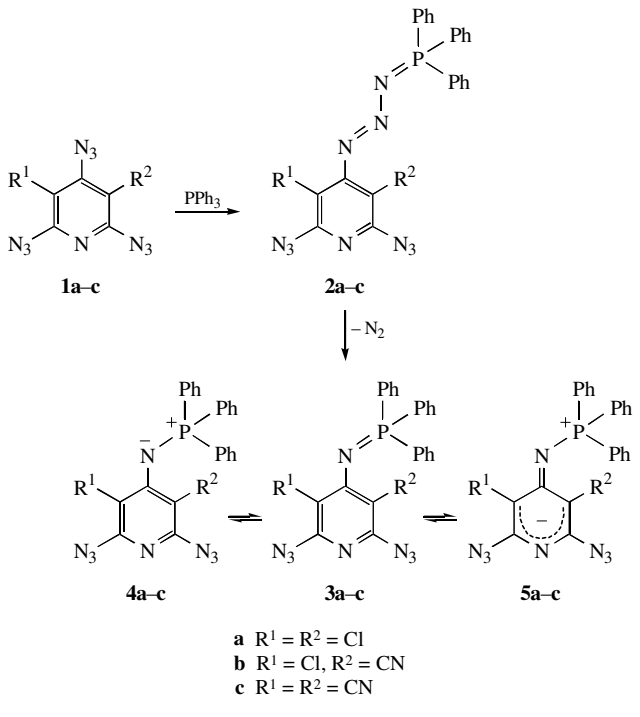
Selective derivatization of the azide groups in polyazides is of considerable interest. Recently we have shown[1–3] that 2,4,6-triazidopyridines **1a–c** add electron-rich dipolarophiles to the azido group at the 4-position of the pyridine ring, whereas in reactions with electron-deficient dipolarophiles cycloadducts are formed at the azido groups in the 2- and 6-positions. To extend the synthetic methods of selective derivatization of the azido groups in 2,4,6-triazidopyridines, the nucleophilic additions of triphenylphosphine (Staudinger reaction[4]) to the azido groups of **1a–c** were studied.

In the reactions† of **1a–c** with an equimolar amount of PPh_3 in diethyl ether at 0 °C, only iminophosphoranes **3a–c** were formed as the final products in quantitative yields. The structures of **3a–c** are supported by the data of elemental analysis and spectroscopic investigations.‡ Thus, for instance, the presence of only three signals at δ 111.5 (d, $^3J_{PC}$ 10.2 Hz), 147.0 (s) and 155.2 (d, $^2J_{PC}$ 3.6 Hz) ppm for the carbon atoms of the pyridine ring in the ^{13}C NMR spectrum of **3a** unambiguously indicates that the addition of a molecule of PPh_3 to triazide **1a** occurs regioselectively at the -azido group. Based on literature analogies,[4] it seems reasonable to assume that the mechanism of the reactions involves initial nucleophilic attack by a molecule of PPh_3 on the azide terminus in the -azido group of **1a–c** and formation of phosphazides **2a–c** as intermediate products. Compounds **2a–c** are obviously unstable at 0 °C and readily lose a molecule of nitrogen to form **3a–c**. The reason for the selective nucleophilic addition of PPh_3 to the -azido groups of **1a–c** can be rationalised from the analysis of the charge distribution in the azido groups of starting triazides. Thus, as can be seen in Table 1, the -azido groups of **1a–c** have the most electrophilic azide termini. By comparing the charges at the azido groups of **1a–c** and their derivatives **3a–c** (Table 1), one can also find that the transformation of the -azido groups of **1a–c** into a strong electron-donating N=PPh_3 substituent leads to a decrease in the electrophilicity of azide termini in the -azido groups of pyridines. Therefore, no surprise that the addition of PPh_3 to all three azido groups of **1b** has been achieved only on prolonged boiling of the reaction mixture in a benzene solution.[7]

Table 1 The charge distribution on the N atoms in azido groups of **1a–c** and **3a–c** computed by the PM3 and RHF/3-21 G* methods.[5,6]

Compound	2-N_3		4-N_3		6-N_3	
	PM3	3-21 G*	PM3	3-21 G*	PM3	3-21 G*
1a	–0.30	—	–0.28	—	–0.30	—
1b	–0.28	0.10	–0.26	0.14	–0.28	0.10
1c	–0.27	0.11	–0.24	0.15	–0.26	0.11
3a	–0.34	—	—	—	–0.33	—
3b	–0.32	—	—	—	–0.32	—
3c	–0.31	—	—	—	–0.31	—

To our knowledge, compounds **3a–c** are the first representatives of azides containing an active phosphaza group in the molecule. According to PM3 computations, among three resonance forms **3**, **4** and **5** the last one most closely fits the structure of such compounds. This conclusion is in full accord with the published data[8,9] on the structure of aryliminophosphoranes. Taking into account the fact that azido and phosphaza groups can be easily modified in numerous fashions[4,10] into other N-containing functions, compounds **3a–c** can be considered as very promising synthons for the preparation of novel pyridine derivatives.



† *A typical procedure for the synthesis of 2,6-diazido-4-iminophosphoranopyridines* **3a–c**. A diethyl ether solution of triphenylphosphine (2 mmol, 50 ml) was added dropwise to a solution, cooled at 0 °C, of triazide **1a–c** (2 mmol) in 100 ml of the ether with stirring. The mixture was kept at 0 °C for 1 h and then warmed to room temperature. The solvent was evaporated under reduced pressure, and the solid residue was recrystallised from hexane. Yields (%): **3a**, 93; **3b**, 95 and **3c**, 97.

‡ *Characteristic data for* **3a**: mp 151–152 °C (decomp.). ^1H NMR ($CDCl_3$) δ: 7.47 (m, 6H, $C_{3'}$–H), 7.55 (m, 3H, $C_{4'}$–H), 7.77 (m, 6H, $C_{2'}$–H). ^{13}C NMR ($CDCl_3$) δ: 111.5 (d, C-3, C-5, $^3J_{PC}$ 10.2 Hz), 128.5 (d, C-3′, $^3J_{PC}$ 13.1 Hz), 131.4 (d, C-1′, $^1J_{PC}$ 106.1 Hz), 131.9 (d, C-4′, $^4J_{PC}$ 2.2 Hz), 132.4 (d, C-2′, $^2J_{PC}$ 10.2 Hz), 147.0 (s, C-2, C-6), 154.5 (d, C-4, $^2J_{PC}$ 3.6 Hz). IR (KBr, ν/cm^{-1}): 2140 (N_3), 1630 and 1570 (C=N, C=C). Found (%): C, 54.86; H, 3.17; N, 22.01; P 5.88. Calc. for $C_{23}H_{15}Cl_2N_8P$ (%): C, 54.68; H, 2.99; N 22.17; P, 6.13.

3b: mp 176–177 °C (decomp.). ^1H NMR ($CDCl_3$) δ: 7.46 (m, 6H, $C_{3'}$–H), 7.53 (m, 3H, $C_{4'}$–H), 7.75 (m, 6H, $C_{2'}$–H). ^{13}C NMR ($CDCl_3$) δ: 92.3 (d, C-5, $^3J_{PC}$ 15.2 Hz), 108.5 (d, C-3, $^3J_{PC}$ 7.3 Hz), 115.8 (C≡N), 128.6 (d, C-3′, $^3J_{PC}$ 13.1 Hz), 130.5 (d, C-1′, $^1J_{PC}$ 106.1 Hz), 131.9 (d, C-4′, $^4J_{PC}$ 2.2 Hz), 132.3 (d, C-2′, $^2J_{PC}$ 10.2 Hz), 152.0 (s, C-6), 154.1 (s, C-2), 159.2 (d, C-4, $^2J_{PC}$ 2.2 Hz). IR (KBr, ν/cm^{-1}): 2225 (C≡N), 2145 (N_3), 1640 and 1565 (C=N, C=C). Found (%): C, 58.32; H, 3.28; N, 27.98; P 6.04. Calc. for $C_{24}H_{15}ClN_9P$ (%): C, 58.14; H, 3.05; N 28.24; P, 6.25.

3c: mp 190–191 °C (decomp.). ^1H NMR ($CDCl_3$) δ: 7.56 (m, 6H, $C_{3'}$–H), 7.67 (m, 3H, $C_{4'}$–H), 7.80 (m, 6H, $C_{2'}$–H). ^{13}C NMR ($CDCl_3$) δ: 89.8 (d, C-3, C-5, $^3J_{PC}$ 12.4 Hz), 115.1 (C≡N), 128.9 (d, C-3′, $^3J_{PC}$ 13.1 Hz), 129.0 (d, C-1′, $^1J_{PC}$ 106.1 Hz), 132.5 (d, C-2′, $^2J_{PC}$ 10.9 Hz), 132.7 (d, C-4′, $^4J_{PC}$ 2.2 Hz), 159.1 (s, C-2, C-6), 163.4 (d, C-4, $^2J_{PC}$ 2.2 Hz). IR (KBr, ν/cm^{-1}): 2230 (C≡N), 2150 (N_3), 1640 and 1565 (C=N, C=C). Found (%): C, 61.97; H, 3.32; N, 28.55; P 6.16. Calc. for $C_{25}H_{15}N_{10}P$ (%): C, 61.74; H, 3.11; N 28.78; P, 6.37.

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