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

Sergei V. Chapyshev

Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax: +7 096 515 3588; e-mail: chap@icp.ac.ru

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

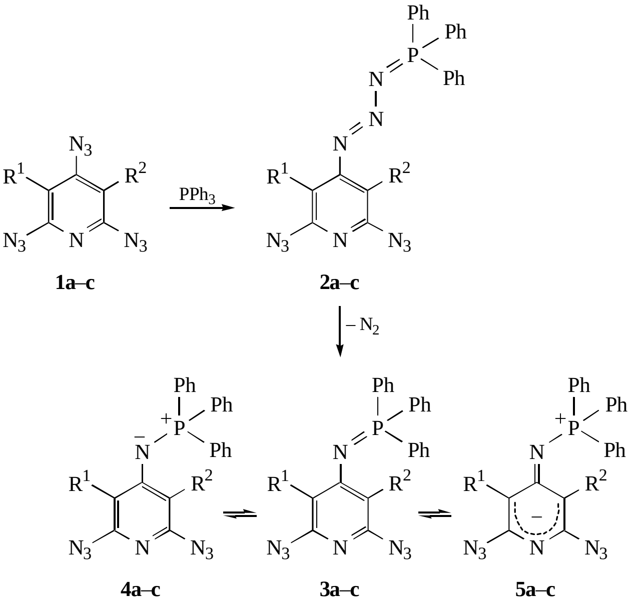
Selective derivatization of the azide groups in polyazides is of considerable interest. Recently we have shown[1–3] that 2,4,6-triazidopyridines **1a**–**c** add electron-rich dipolarophiles to the azido group at the 4-position of the pyridine ring, whereas in reactions with electron-deficient dipolarophiles 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 γ-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 γ-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 γ-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 γ-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 γ-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 α-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_γ atoms in azido groups of **1a**–**c** and **3a**–**c** computed by the PM3 and RHF/3-21 G* methods.[5,6]

Compound	$2\text{-}N_3$		$4\text{-}N_3$		$6\text{-}N_3$	
	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 $R^1 = R^2 = Cl$
b $R^1 = Cl$, $R^2 = CN$
c $R^1 = R^2 = CN$

[†] *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.

References

1 S. V. Chapyshev, U. Bergstrasser and M. Regitz, *Khim. Geterotsikl. Soedin*., 1996, 67 [*Chem. Heterocycl. Compd*. (*Engl. Transl*.), 1996, **32**, 59].

2 S. V. Chapyshev and V. M. Anisimov, *Khim. Geterotsikl. Soedin*., 1997, 1521 [*Chem. Heterocycl. Compd*. (*Engl. Transl*.), 1997, **33**, 1315].

3 S. V. Chapyshev, *Mendeleev Commun*., 1999, 164.

4 (*a*) Yu. G. Gololobov, I. N. Zhmurova and L. F. Kazukhin, *Tetrahedron*, 1981, **37**, 437; (*b*) Yu. G. Gololobov and L. F. Kazukhin, *Tetrahedron*, 1992, **48**, 1353.

5 (*a*) J. J. P. Stewart, *J. Comput. Chem*., 1989, **10**, 209; (*b*) *Spartan version 4.0*, Wavefunction, Inc., USA, 1995.

6 M. W. Schmidt, K. K. Baldrige, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. J. Su, T. L. Windus, M. Dupius, J. A. Montgomery, *J. Comput. Chem*., 1993, **14**, 1347.

7 S. V. Chapyshev and T. Ibata, *Heterocycles*, 1993, **36**, 2185.

8 M. Pomerantz, D. S. Marynick, K. Rajeshwar, W.-N. Chou, L. Throckmorton, E. W. Tsai, P. C. Y. Chen and T. Cain, *J. Org. Chem*., 1986, **51**, 1223.

9 T. A. Albright, W. J. Freeman and E. E. Schweizer, *J. Am. Chem. Soc*., 1975, **97**, 940.

10 E. Scriven and K. Turnbull, *Chem. Rev.*, 1988, **88**, 297.

Received: 4th March 1999; Com. 99/1457