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SYNTHESIS AND REGIOSELECTIVE CYCLOADDITION REACTION OF 2,4,6-TRIAZIDO-3-CHLORO-5-CYANOPYRIDINE WITH NORBORNENE

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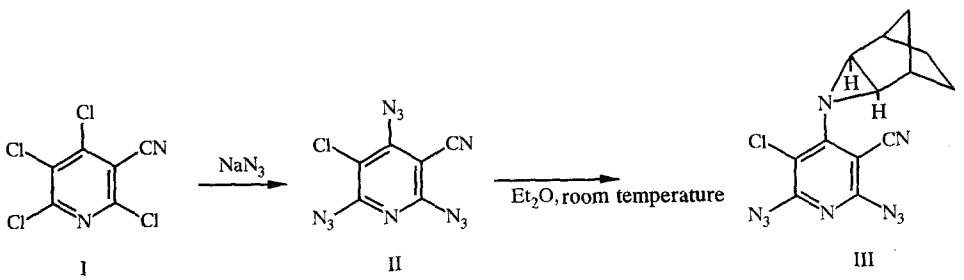
Treatment of 3-cyanotetrachloropyridine with sodium azide gives 2,4,6-triazido-3-chloro-5-cyanopyridine. This compound reacts regioselectively with norbornene to form an aziridinyl cycloadduct only at the azido group in position 4 of the pyridine ring.

Thanks to the ability of an azide group to undergo a range of transformations to other nitrogen functions [1], azidopyridines can prove to be promising starting materials for the synthesis of variously substituted pyridines. However, the chemistry of triazidopyridines remains almost unexplored at this time. It has been noted [2] that one possible route to triazidopyridines may be the reaction of polychloropyridines with sodium azide. However, the authors could only obtain 2-azido-5-cyano-trichloropyridine when treating 3-cyanotetrachloro-pyridine with sodium azide in refluxing DMF [2].

The aim of this work was to study the possible occurrence of triazidopyridines in the reaction of 3-cyanotetrachloropyridine with sodium azide and to study the reactivity of these triazidopyridines through their reaction with norbornene.



I II III

In the reaction of I with excess sodium azide it was found that, in aqueous acetone, I readily undergoes nucleophilic substitution of the three chlorine atoms in positions 2, 4, and 6 of the pyridine ring, even in very mild conditions (5°C). The yield of triazidopyridine II was 88%.

The composition and structure of II fully agreed with elemental analytical, IR, and ^{13}C NMR spectroscopic data. Hence, in the IR spectrum of II there are observed both a 2230 cm^{-1} absorption for the C=N group and three strong bands at 2140, 2120, and 2070 cm^{-1} assigned to the three azide groups. It was also of interest to measure the ^{13}C NMR spectrum of II since azide groups alpha to nitrogen in a pyridine ring can take part in azidotetrazole tautomerism [1]. It is known that formation of the tetrazole tautomer can be identified in the ^{13}C NMR of an azidopyridine through a significant high field shift (to 130-120 ppm) for the pyridine alpha carbon atom not involved in formation of the tetrazole ring [3]. Also, a study of the ^{13}C NMR spectrum of II in the temperature range −20 to 50°C showed that the chemical shifts of the signals for carbons 2 and 6 were virtually unaffected by temperature and occurred at 154.5 and 154.0 ppm. This is consistent with a powerfully electron accepting effect for all five substituents in the pyridine ring of triazidopyridine II causing it to occur only in the azido form.

The presence of three azide groups in II is of interest in showing how the reactivity of the azide group depends on its position in the pyridine ring. As a model we have chosen the reaction of II with such strong dipolarophiles as norbornene [4] which does not rule out the participation of all three azide groups in the cycloaddition reaction.

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The reaction was carried out in the dark at room temperature using ether solvent. The only reaction product is the cycloadduct III (90% yield) which results from addition of norbornene only at the 4 position in II. As in the case of 4-azidotetrachloropyridine [5], the reaction of II with norbornene does not stop at the triazoline ring formation stage but continues with elimination of a nitrogen molecule to form the aziridine cycloadduct. As might be expected [5, 6], cycloadduct III has the more favorable exo- conformation. This is indicated by the absence of spin–spin interaction between the aziridine ring and bridgehead CH protons of the aliphatic fragment of III which shows two singlets at 2.90 and 2.73 ppm in its proton NMR spectrum.

The regioselective cycloaddition of II we have describd can be used as a synthetic method for the selective reaction of azide groups in a triazidopyridine.

EXPERIMENTAL

IR spectra were recorded on a Specord IR-75 instrument and PMR spectra on a Bruker AC-200 instrument using TMS internal standard. ^{13}C NMR spectra were obtained on a Bruker AM-400 (100.6 MHz) instrument. The reaction and compound purities were monitored by TLC using Silufol UV-254 plates in ethyl acetate–benzene (1:3).

Elemental analytical data for C, H, and N for II and III agreed with that calculated.

2,4,6-Triazido-3-chloro-5-cyanopyridine (II, C_6ClN_1). Sodium azide (2.6 g, 40 mmole) in water (10 ml) was added to a solution of I (2.42 g, 10 mmole) in aqueous acetone (200 ml, 10% water). The mixture was stirred in the dark at room temperature for 6 h, the solvent distilled off, and water (200 ml) added to the residue. The precipitate was filtered, washed with water, and recrystallized from ethanol. Drying gave II (2.3 g, 88%) with mp 65°C. IR Spectrum: 2230 (C=N), 2140, 2120, 2070 cm^{-1} (N_3). ^{13}C NMR Spectrum ($CDCl_3$): 154.5 (C_2); 154.0 (C_6); 149.0 (C_4); 110.0 (C=N); 107.9 (C_3); 87.9 ppm (C_5).

3-(2,6-Diazido-3-chloro-5-cyano-4-pyridyl)-3-azatricyclo-[3.2.1.0]octane (III, $C_{13}H_{10}ClN_9$): Norbornene (0.38 g, 4 mmole) in ether (30 ml) was added to a solution of II (0.26 g, 1 mmole) in dry ether (200 ml). The product was held in the dark at room temperature for 2 weeks after which the solvent was removed in vacuo. The residue was recrystallized from alcohol to given III (0.3 g, 90%) with mp 166-167°C. IR Spectrum: 2224 (C≡N), 2150, 2130 cm^{-1} (N≡N). PMR Spectrum ($CDCl_3$): 0.94 (1H, d, J = 11 Hz, 8-H_{endo}); 1.32 (3H, m, 8-H_{exo}, 6- and 7a-H); 1.58 (2H, m, 6- and 7e-H); 2.73 (2H, s, H_{bridge}); 2.90 ppm (2H, s, NCH). ^{13}C NMR Spectrum ($CDCl_3$): 25.6 (CH_2-CH_2); 28.7 ($CH-CH_2$); 36.8 (CH); 43.8 (NCH); 86.6 (C_5); 105.7 (C_3); 112.7 (C≡N); 152.9 (C_6); 154.7 (C_2); 159.6 ppm (C_4).

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