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THE CHEMISTRY OF CYANOACETYLENES XIII DIELS-ALDER REACTIONS OF 6-CHLORO-3-CYANO-2,4-BIS(DIMETHYLAMINO)PYRIDINE WITH ELECTROPHILIC ACETYLENES

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For further investigation on the chemical behaviors of the cycloadducts of N,N-dialkylaminocyanoynamines to hydrogen chloride (1), 6-chloro-3-cyano-2,4-bis(dimethylamino)pyridine (I), one of the adducts, was treated with cyanoacetylene in carbon tetrachloride in a sealed tube at 90-100° in the presence of a small amount of aluminium chloride (2) for 5 days afforded 4% yield of pale yellow needles (II), m.p. 281-284°, together with over 60% recovery of I. The analysis showed a chemical formula of $C_{13}H_{13}N_5$, corresponding to that of the elimination of hydrogen chloride from the 1:1 adduct of I to the acetylene. The spectral data manifested the existence of one aromatic proton (at δ 7.64 (1H, s) in the NMR and at 3030 cm^{-1} in the IR spectrum), two equivalent dimethylamino groups (at δ 3.31 (12H, s) in the NMR spectrum) and at least two nonequivalent cyano groups (at 2260 and 2240 cm^{-1} in the IR spectrum). From such a symmetrical pattern similar to 2,4-bis(diethylamino)-1,3,5-carbomethoxybenzene (3), the structure of II was assigned as 2,4-bis(dimethylamino)-1,3,5-tricyanobenzene.

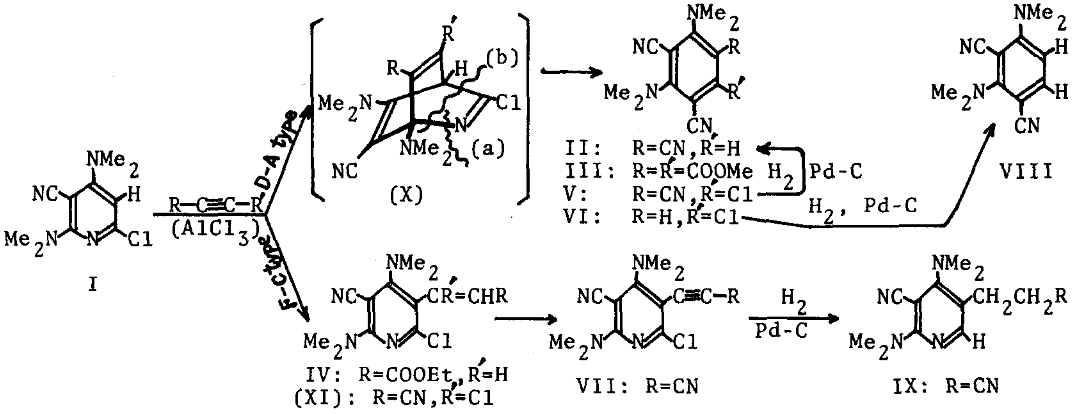
Similar treatment of I with dimethyl acetylenedicarboxylate at 110° for 4 days but in the absence of aluminium chloride afforded 65% yield of pale yellow crystals (III), m.p. 178-179°; the analysis showed $C_{14}H_{18}N_4O_4$ (1:1 adduct minus hydrogen chloride). From the NMR (two nonequivalent carbomethoxy groups at δ 3.91 (3H, s) and 3.79 (3H, s) and dimethylamino groups at δ 3.26 (6H, s) and 3.03 (6H, s)), IR (carbonyl at 1735 and cyano groups at 2250 cm^{-1}) and furthermore, the UV spectrum (λ_{max}^{EtOH}nm (log ε): 384 (3.94), 287 (4.54) and 208 (4.35)) similar to II (381 (3.96), 288 (4.66) and 211 (4.39)), the structure was concluded to be 1,3-bis(dimethylamino)-2,4-dicyano-5,6-carbomethoxybenzene.

Treatment of I with ethyl propiolate in the presence of aluminium chloride under reflux in chloroform for 5 days furnished 68% yield of an almost colorless crystalline product (IV), m.p. 119-120°; the analysis showed $C_{15}H_{19}N_4O_2Cl$, 1:1 adduct. The remarkable difference in the UV spectrum (λ_{max}^{EtOH} nm (log ε): 341 (4.18), 293 (4.36) and 216 (4.73)) from those of II and III, but rather similar to I (336 (4.00), 256 (4.52) and 212 (4.38)), especially at the longest wavelength suggests the presence of a pyridine skeleton in IV rather than benzene. The NMR signals due to two nonequivalent dimethylamino groups at δ 3.22 (6H, s) and 3.03 (6H, s), two trans-olefinic protons at δ 7.68 (1H, d, 16.5 Hz) and 6.02 (1H, d, 16.5 Hz) and one carboethoxy group at δ 4.23 (2H, q, 7.0 Hz) and 1.32 (3H, t, 7.0 Hz) and the IR absorptions of olefinic at 1630, carbonyl at 1708, and cyano groups at 2240 cm^{-1} support the structure to be 6-chloro-5-(trans-2-carboethoxyethenyl)-3-cyano-2,4-bis(dimethylamino)pyridine.

The reaction of I with chlorocyanoacetylene in carbon tetrachloride in a sealed tube at 95-105° for 4 days in the presence of aluminium chloride afforded 80% overall yield of a mixture of three crystalline products V, VI and VII with the ratio of 10:3:4 on the g.l.c. inspection. Separation of these products were successfully carried out by column chromatography (Mallinckrodt 100 mesh silicic acid and chloroform as an eluent). Compound V, m.p. 267-268°, was determined to have a chemical formula of $C_{13}H_{12}N_5Cl$ (M^+: 273) on the basis of the analysis and mass spectrum, which corresponds to a 1:1 adduct minus hydrogen chloride. From the spectral resemblance (two eqivalent dimethylamino groups at δ 3.31 (12H, s) in the NMR, cyano groups at 2250 cm^{-1} in the IR spectrum and the UV absorptions (λ_{max}^{EtOH} nm (log ε): 384 (3.95), 292 (4.71), 228 (4.34), and 215 (4.32)) to II, the structure was concluded to be 1,3,5-tricyano-2,4-bis(dimethylamino)-6-chlorobenzene, which was further confirmed by the following chemical evidence: the hydrogenation of V over palladium on charcoal at room temperature for 30 min furnished II in 49% yield in addition to recovered V. Compound VI, m.p. 201-202°, showed a chemical formula of $C_{12}H_{13}N_4Cl$ (M^+: 248), 1:1 adduct minus cyanogen chloride, from the analysis and the mass spectrum. The NMR spectrum manifested one aromatic proton at δ 6.37 (1H, s) and two nonequivalent dimethylamino groups at δ 3.22 (6H, s) and 3.12 (6H, s) and the IR spectrum indicated the existence of nitrile groups at 2250 cm^{-1}. From these data and the UV spectral resemblane (λ_{max}^{EtOH} nm (log ε): 367 (3.98), 273 (4.56), and 226 (4.32)) to II and III, the structure was assigned to 6-chloro-2,4-bis(dimethylamino)-1,3-dicyanobenzene. Hydrogenation of this compound VI over palladium on charcoal at room temperature for 15 hr afforded 81% yield of colorless crystals (VIII), m.p. 111-112°, a chemical formula of which was given as $C_{12}H_{14}N_4$ based on the analysis, an indicative of the substitution of the chlorine atom in VI with hydrogen. In the NMR spectrum, two vicinal aromatic protons at δ 7.26 (1H, d, 9.0 Hz) and 6.23 (1H, d, 9.0 Hz) were observed in addition to two nonequivalent dimethylamino groups at δ 3.19 (6H, s) and 3.10 (6H, s), while in the IR spectrum, the nitrile absorption at 2250 cm^{-1} remained unchanged. Thus, the structure of VIII was characterized as 2,4-bis(dimethylamino)-1,3-dicyanobenzene. As for compound VII, m.p. 173-174°, the same chemical formula of $C_{13}H_{12}N_5Cl$ (M^+: 273) as V was given on the basis of the analysis and the mass spectrum, but the spectra were quite different from V; the NMR spectrum showed two nonequivalent dimethylamino groups at δ 3.28 (6H, s) and 3.26 (6H, s), the IR spectrum manifested two nonequivalent cyano groups at 2260 and 2240 cm^{-1} in addition to an acetylenic group at 2150 cm^{-1} and the UV absorptions appeared at 360 nm (log ε: 4.10), 320 (4.33), and 213 (4.31) in ethanol, which resembled to those of IV rather than to those of V, indicating the presence of a pyridine skeleton and the structure was assigned to 5-(2-cyanoethynyl)-3-cyano-2,4-bis(dimethylamino)pyridine. This compound (VII) was hydrogenated over palladium on charcoal at room temperature for 18 hr to afford 68% yield of a crystalline product (IX), m.p. 92-95°. In the IR spectrum, the acetylenic absorption at 2150 cm^{-1} was no more observed and a chemical formula of IX was given as $C_{13}H_{17}N_5$ from the analysis, indicating that the saturation of the acetylenic linkage and the substitution of the chlorine atom with hydrogen had occurred in the hydrogenation of VII. This was demonstrated in the NMR that showed new appearance of one aromatic proton at δ 7.92 (1H, s) and four $-CH_2CH_2-$ protons at δ 2.9-2.5 (4H, m, A_2B_2-pattern) in IX. Thus, the structure was assigned as 5-(2-cyanoethyl)-3-cyano-2,4-bis(dimethylamino)pyridine.

The reason why different types of the reactions were observed according to the structures of the acetylenic derivatives, though similar reactions of diethyl 2,4-bis(diethylamino)cyclobutadiene-1,3-dicarboxylate with propiolate and acetylenedicarboxylate afford the same types of the benzene derivatives (3), is uncertain, but the mechanism for the conversion of a pyridine derivative (I) into benzene derivatives (II), (III), (V), and (VI) with electrophilic acetylenes under thermal Diels-Alder reaction conditions might be explained by assuming the intermediate formation of the Diels-Alder adducts (X), followed by the carbon-nitrogen bond cleavage (a) and aromatization by the elimination of hydrogen chloride to II, III, and V or of cyanogen chloride to VI by the cleavage (b) as shown in a Scheme. Compound IV might be the Friedel-Crafts product from I and propiolate in the presence of alminium chloride and similarly, the side-formation of VII could be elicited by the intermediate formation of the Friedel-Crafts product (XI), followed by the elimination of hydrogen chloride (4).

This is the first example of the Diels-Alder reactions of the pyridine derivatives with electrophilic acetylenes (5).



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