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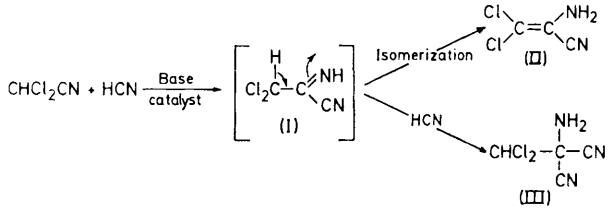
ββ-Dichloro-α-aminoacrylonitrile

By Koichi Matsumura, Takahiro Saraie, and Naoto Hashimoto*

(*Chemical Research Laboratories, Research and Development Division, Takeda Chemical Industries, Ltd., Juso-Nishino-cho, Higashiyodogawa-ku, Osaka, Japan*)

Summary Dichloroacetonitrile reacts with HCN to give the title compound, an enamine, acylation of which, followed by treatment with amines, provides a new synthesis of oxazoles.

We have reported previously the synthesis of ββ-dichloroacrylonitrile by the co-pyrolysis of acetonitrile and carbon tetrachloride. We now describe a novel synthesis of the α-aminoacrylonitrile (II) by base-catalysed addition of HCN to dichloroacetonitrile.



HCN adds to the triple bond of CCl_3CN, $MeCCl_2CN$,[2] some perfluoronitriles[3] and cyanogen[4] to give α-iminonitriles. Similar addition of HCN can be presumed to operate in an adenine synthesis which uses HCN as one of the starting materials.[5]

For the addition to be successful, the cyano-group must apparently be activated by one, or usually more than two, strongly electron-withdrawing groups on the α-carbon atom. Addition of HCN to nitriles having hydrogen atoms on the α-carbon atom occurs in only a few special cases: *e.g.*, the formation of a tetramer of HCN,[6] and reactions of aminomalononitrile toluene-*p*-sulphonate[7] and ethyl α-cyanopropionate[8] with cyanide ion. We have found that reaction of $CHCl_2CN$ with HCN (1·1 mol. equiv.) in the presence of a catalytic amount of NaCN in MeCN at room temperature gives a 1:1 adduct as needles, m.p. 61°, (96%).

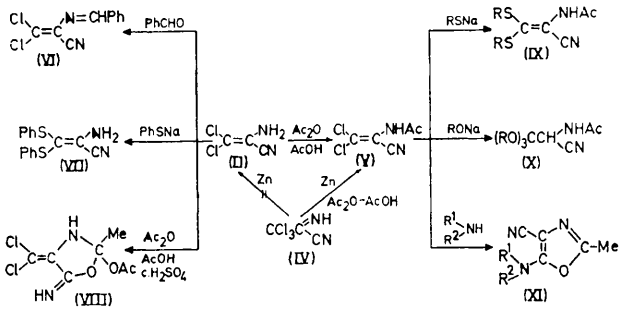
HCN could successfully be replaced by acetone cyanohydrin for safety in handling. Evidence that the 1:1 adduct has the enamine structure (II) and not the imine structure (I) came from a comparison of the i.r., n.m.r., and u.v. spectra of the adduct with those of (IV), which was prepared by the addition of HCN to CCl_3CN.

Thus, the i.r. spectrum of (IV) shows absorptions at 3230 (NH), 2250 (C≡N), and 1634 cm^{-1} (C═N), in contrast to that of (II): 3484, 3384, 3200 (NH_2), 2247 (C≡N), and 1618 cm^{-1} (C═C). The n.m.r. spectrum of (IV) ($CDCl_3$) shows two resonances: δ 11·36 and 11·84 p.p.m. (2:1) (NH), but that of (II) ($CDCl_3$) only one: δ 3·67br p.p.m. (NH_2). Although the λ_{max} values in the u.v. spectra of (IV) and (II) are nearly equal (260·0 and 260·5 nm, respectively), the extinction coefficient of (IV) (ε 177) is different from that of (II) (9300).

In addition, the reductive acetylation of (IV) gave the acetylated product (V) (58%), identical with the compound derived from (II). When excess of HCN was used in the present reaction, a 1:2 adduct (III) (oil) was isolated, the structure of which was supported by its i.r. and n.m.r. spectra. This is presumably formed by addition of HCN to the imino group of (I), because it was not obtained by reaction of (II) with HCN under similar conditions. Similarly, dibromoacetonitrile reacted with HCN to give ββ-dibromo-α-aminoacrylonitrile, m.p. 76—77° (82%), the structure of which was proved by its i.r., n.m.r., and mass spectra, elemental analysis and the formation of acetyl and Schiff base derivatives. ββ-Dihalogeno-α-aminoacrylo-

nitriles, although easily purified by recrystallization from light petroleum, decompose gradually in the air at room temperature. They can be stored without significant change for a long period under nitrogen or in a solvent such as ether.

The acrylonitriles (II) and (V) are highly reactive polyfunctional compounds, and are useful starting materials for the synthesis of oxazoles and other compounds (Scheme).



SCHEME

Reaction of (II) with benzaldehyde gives (VI), m.p. 78—79° (96%). Two chlorine atoms of (II) are easily replaced by thiophenolate to give (VII), m.p. 92° (83%). Reaction of (II) with Ac_2O–AcOH gives (V), m.p. 128—130° (95%), whereas a cyclized product (VIII), m.p. *ca.* 165° (decomp.), is obtained (86%), when a catalytic amount of conc. H_2SO_4 is added to the Ac_2O–AcOH mixture.

Compound (V) reacts with thiols in the presence of bases to give (IX) (R = Me: m.p. 115°; R = Et: m.p. 87°; R = Ph: m.p. 110°) in good yields. Reaction of (V) with sodium alkoxides gives (X) (R = Me: m.p. 91—92°; R = Et: m.p. 103—105°). With primary and secondary amines and hydrazines, (V) reacts readily to give oxazole derivatives (XI) (R^1 = Me, R^2 = H: oil; R^1 = $PhCH_2$, R^2 = H: m.p. 82—83·5°; R^1,R^2 = morpholino: m.p. 81—82°; R^1 = NH_2, R^2 = H: m.p. 163—165°) in almost quantitative yield.

The reaction is useful for the synthesis of 4-cyano-5-(*N*-substituted amino)-oxazoles.

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