Potential Antiradiation Drugs: α-Alkyloximinonitriles

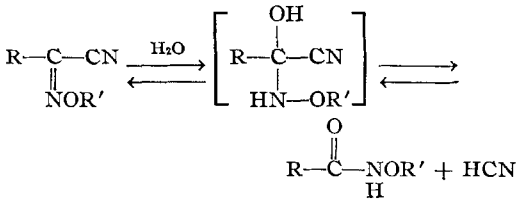
By DOMINICK A. COVIELLO

Of three α-alkyloximinonitriles tested for radiation protection, two were very toxic and inactive, while one with low toxicity gave slight protection.

MANY classes of compounds including nitriles have shown varying degrees of protection against radiation damage in mammals. It has been suggested that conceivably the nitriles act by the slow sustained-release of HCN which is protective (1). If the theory has merit, it was postulated that α-alkyloximinonitriles, reacting with water in the cellular milieu, could yield an intermediate which would decompose to yield HCN and an *O*-alkylhydroxamic acid according to Scheme I.

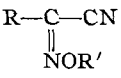
It is interesting to note (Table I) that 1-benzyloximinobutanecarbonitrile gives slight protection, and has an LD_{50} of about 1000 mg./Kg. while the other two, 1-benzyloximinopropanecarbonitrile and 1-benzyloximinoheptanecarbonitrile, give no protection with LD_{50}'s of less than 50 mg./Kg.

Some of the nitriles were previously reported (2). The new compounds were characterized by the characteristic nitrile absorption in the infrared (3) and by alkaline hydrolysis back to the starting acids. They are shown in Table II.



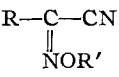
Scheme I

TABLE I.—α-ALKYLOXIMINONITRILES TESTED FOR RADIATION PROTECTION



Compd. R	Compd. R′	LD_{50}, mg./Kg.	Test Dose, mg./Kg.	Test Evaluation
CH_3	$C_6H_5CH_2$	Less than 50	50–150	No protection
			150–350	No protection
C_2H_5	$C_6H_5CH_2$	1000–1500	350–700	No protection
			700–1000	Slight protection
C_5H_{11}	$C_6H_5CH_2$	Less than 50	150–350	No protection
			350–700	No protection

TABLE II.—α-ALKYLOXIMINONITRILES PREPARED



Compd. R	Compd. R′	B.p.	$n_D/t°$	Yield	C—N Stretch cm.$^{-1}$
Methyl	Methyl	132–133/760 mm.	1.4336/20°	54	2230
Methyl	Ethyl	147–148/760 mm.	1.4241/24°	58	2230
Methyl	Benzyl	80–85/0.03 mm.	1.3815/26°	21	2236
Ethyl	Ethyl	166–167/760 mm.	1.4258/28°	60	2230
Ethyl	Benzyl	102–105/0.5 mm.	1.5179/25°	17	2235
Butyl	Methyl	84–85/15 mm.	1.4300/25°	55	2240
Butyl	Ethyl	87–89/15 mm.	1.4325/26°	50	2240
Butyl	Benzyl	96–98/0.01 mm.	1.5087/25°	45	2240
Amyl	Benzyl	123–125/0.1 mm.	1.475/6°	29	2248

The amide precursors for the nitrile preparation have been reported (4).

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