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ARYLGLYOXYLIC ACIDS FROM α-AZIDOARYLACETIC ACIDS

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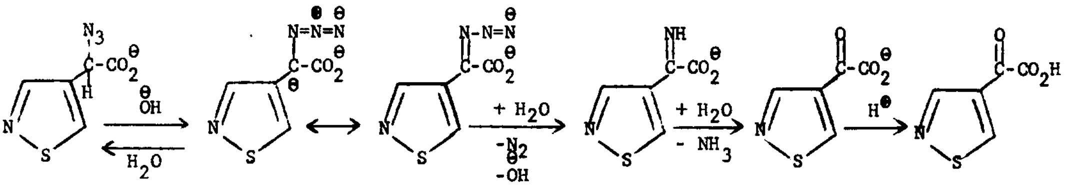
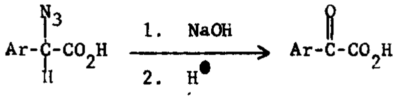
An attempt to racemize optically active α-azido-4-isothiazolylacetic acid (1) by treatment with dilute aqueous sodium hydroxide led to the discovery of an interesting synthesis of arylglyoxylic acids. When 0.050 mole of α-azido-4-isothiazolylacetic acid was treated at room temperature with 50 ml of 3N aqueous sodium hydroxide an exothermic reaction took place with concomitant gas evolution and ammonia formation. From the reaction mixture sodium 4-isothiazolylglyoxylate separated as a white solid, which upon acidification yielded 4-isothiazolylglyoxylic acid (77%), m.p. 155-157°; νmax(Nujol) 1720 and 1680 cm^{-1}; the n.m.r. spectrum (in $D_2O + K_2CO_3$) contained singlets at τ0.44 and 1.17 of equal intensity. The reaction can be explained by the following mechanism:



The unexpected outcome of the reaction prompted us to subject some other α-azidoarylacetic acids (2,3) to treatment with three equivalents of either 3N aqueous sodium hydroxide or 3N methanolic sodium hydroxide. α-Azidophenylacetic acid had to be heated at 50° for 16 h with aqueous NaOH for the nitrogen evolution to be complete; with methanolic NaOH the reaction was considerably faster. Phenylglyoxylic acid was isolated in 61 and 69% yield respectively after acidification and extraction with ether. Similarly were prepared: p-chlorophenylglyoxylic acid, 1-naphthylglyoxylic acid and 3-thienylglyoxylic acid. Table I lists the yields and reaction conditions of the arylglyoxylic acids prepared by this method. The good yields generally obtained make this method useful for the preparation of certain arylglyoxylic acids, such as 3-thienylglyoxylic acid and 4-isothiazolylglyoxylic acid, which are difficult to prepare otherwise.

Table I

Arylglyoxylic acids[a] prepared from α-azidoarylacetic acids



$$\mathrm{Ar}\text{-}\overset{N_3}{\underset{H}{C}}\text{-}CO_2H \xrightarrow[2.\ H^{\bullet}]{1.\ NaOH} \mathrm{Ar}\text{-}\overset{O}{\overset{\|}{C}}\text{-}CO_2H$$

Ar	M.P., °C		with 3N aq. NaOH		with 3N meth. NaOH	
	found	lit.(ref.)	Conditions	% Yield	Conditions	% Yield
C_6H_5	64-67	64-66(4)	16 h at 50°	61	1.5 h at 50°	69
p-ClC_6H_4	92-93	90-91(5)	3 h at 50°	84	16 h at 25°	81
1-naphthyl	111-114	107-108(6)	16 h at 50°	56	-----------	--
3-thienyl[b]	65-67	---------	----------	--	36 h at 25°	77
4-isothiazolyl[c]	155-157	---------	1.5 h at 25°	77	-----------	--

a. The identity of the known acids was proven by direct comparison with authentic samples.

b. Anal. Calcd. for $C_6H_4O_3S$: C, 46.14; H, 2.58; N, 20.53. Found: C, 46.35; H, 2.81; N, 20.85.

c. Anal. Calcd. for $C_5H_3NO_3S$ (mol.wt. 157): C, 38.22; H, 1.93; N, 8.92. Found: C, 38.49; H, 2.04; N, 9.19; neutralization equivalent, 154.

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