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AMBIDENT OXIDATIVE RING CLOSURE OF SEMICARBAZONES

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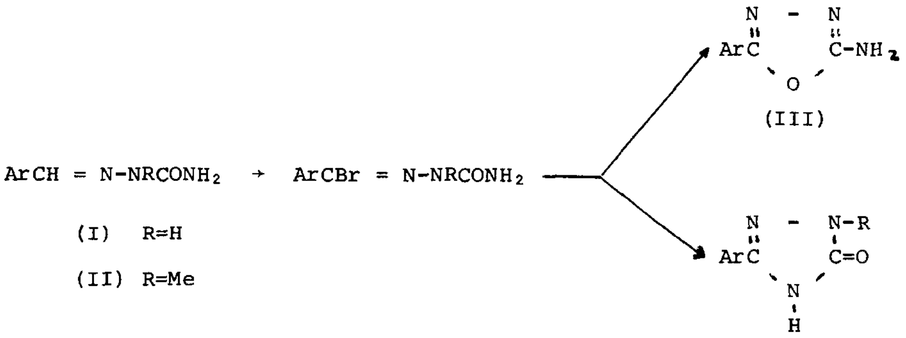
The reactions of arylidene semicarbazones (I) with bromine in acetic acid containing either (or both) sodium acetate[1] or water[2] lead (via oxygen (O)-attack) to oxadiazoles (III), in good (*ca.* 70%) yields with short (20 min.) reaction times at ambient temperatures. We now report the incursion of a new reaction in this system, namely nitrogen (N)-attack yielding triazolones (IV) - a reaction which requires treatment of the semicarbazones (I) with bromine in anhydrous acetic acid over (48 hrs.). This is the best recorded route to such triazolones from semicarbazones - the other method reported[3] (using ferric chloride in ethanol at 120°) is both inconvenient (sealed ampules) and inefficient (yields 10-20%). Our new general reaction procedure involves addition of 20 m.moles of bromine (neat) to a suspension of compound (I) 10 m.moles in 'pronalys' acetic acid at ambient temperature, with stirring for 48 hours. The insoluble triazolone (together with some ammonium bromide) precipitates out. Addition of water to the filtrate precipitates any unchanged starting material and the mother liquor upon basification and work-up yields the corresponding oxadiazoles, (See Table). Performing these reactions in refluxing 'Pronalys" acetic acid decreases the reaction time (to 20 minutes) increases the yields of triazolones (and ammonium bromide) and yields no oxygen closure products. When the products (III) and (IV) were treated under the reaction conditions used for the cyclization of the parent semicarbazones, the products were recovered unchanged, they did not interconvert under the reaction conditions used.



Scheme I (IV)

TABLE

OXIDATIVE CYCLIZATION OF SEMICARBAZONES (I) WITH BROMINE IN ANHYDROUS ACETIC ACID AT 20°C.

Substrate Ar	N-attack (IV)	O-attack (III)	OTHERS		
			NH_4Br	(I)	ArCHO
C_6H_5	51 (58)[a]	7	16 (20)[a]	-	5
$p\text{-}ClC_6H_4$	43 (66)[a]	3	11 (17)[a]	26	-
$p\text{-}BrC_6H_4$	47 (74)[a]	4	12 (16)[a]	23	-
$p\text{-}MeC_6H_4$	42	5	14	13	4
$p\text{-}MeOC_6H_4$	41	7	13	15	-

[a] Results from reactions in refluxing acetic acid.

Adding either sodium acetate or water to bromine in acetic acid influences the reaction with semicarbazones in two ways - rapid acceleration in overall reaction rate together with the exclusion of any N-attack. We envisage that O- and N-attack arise from initial hydrazidic bromination (to form $ArCBr = N\text{-}NHCONH_2$) and these hydrazidic bromides then undergo a duality of reaction. We have established elsewhere[5] that hydrazidic halides undergo both ionization (to yield carbonium ions e.g. $Ar\overset{+}{C}=N\text{-}NHCONH_2$) and 1,3-dipolar elimination (to yield nitrilimines e.g. $Ar\overset{+}{C}=N\text{-}\overset{-}{N}CONH_2$) depending especially upon the pH of the medium. We regard the oxygen attack in base or water (leading to product III) as arising from a 1,5-dipolar addition process involving a nitrilimine, whereas the concurrent nitrogen and oxygen attack in anhydrous acetic acid arises from ambident nucleophilic attack at a carbonium ion centre. As a confirmation of this, reaction of 2-methyl semicarbazones (II, with Ar being C_6H_5, $p\text{-}ClC_6H_4$, $p\text{-}BrC_6H_4$), wherein 1,3-dipolar ion formation is structurally prohibited, with bromine in acetic acid containing base or water did not yield any oxadiazole (III) product. However, when compounds (II) were treated with bromine in refluxing anhydrous acetic acid, they yielded the corresponding triazolones (IV, R=Me) in greater than 70% yield.

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