

BOND ALTERNATION AND MUTAGENICITY OF AZULENOQUINOLINES AND DIAZULENOPYRIDINES

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Many benzenoid aza-arenes have been known to be carcinogenic and mutagenic, but the bioactivity of non-benzenoid aza-arenes containing the azulene ring has been uninvestigated. Azulenobenzoquinolines (2 & 3) and diazulenopyridines (4, 5, and 6) have an isoelectronic structure with carcinogenic dibenzacridines. The synthesis, bond alternation, and mutagenicity of azulenoquinolines and diazulenopyridines will be presented. Ullmann coupling of a mixture of activated 2-chloroazulene derivative (I) and arylamines (aryl=phenyl, α - and β -naphthyl) gave the corresponding arylazuleneamines (II) in good yields. Friedel-Craft ring closure of II with PPA afforded pyridone type compounds (III). Upon heating of III with POCl_3 , aromatization to chloropyridines (IV) was achieved. Finally, dechlorination of IV with hydrazine- PtO_2 generated the target compounds (1, 2, and 3). Diazulenopyridines (4, 5, and 6) were also synthesized by using of 2-aminoazulene derivative as a starting material which was coupled with 2-, 1-, or 6-haloazulenes, respectively. The bond alternation of the azulene ring of 1~6 on the basis of the vicinal coupling constants of their NMR spectra increases in a relative order: 4 > 1 > 6 > 2, 3 > 5. Mutagenicity of 2, 3, and 4 was tested in *Salmonella* typhimurium strains TA 98 and TA 100 with and without rat liver S9 mix. All these compounds were inactive without S9 mix. In the presence of S9 mix, 2 [revertant/ μg = 8] and 3 [7] were as active as dibenz[*c,h*]acridine to TA 98, but 4 [19] was more active than it. Compounds 2 [58], 3 [12], 4 [31] were somewhat weaker to TA 100 than dibenz[*c,h*]acridine [95] and benzo[*a*]pyrene [80]. The difference between 2 and 3 can be explained by π -delocalization energy calculated for substitution of CH_2^+ ion at the positions 4 (0.877 β) or 1 (0.796 β) of azulenoquinoline (1).

