HOMOLYTICAL ALKYLATION OF HETEROAROMATIC BASES BY CYCLIC ACETALS

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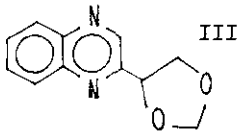
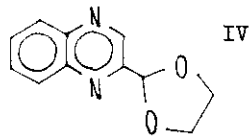
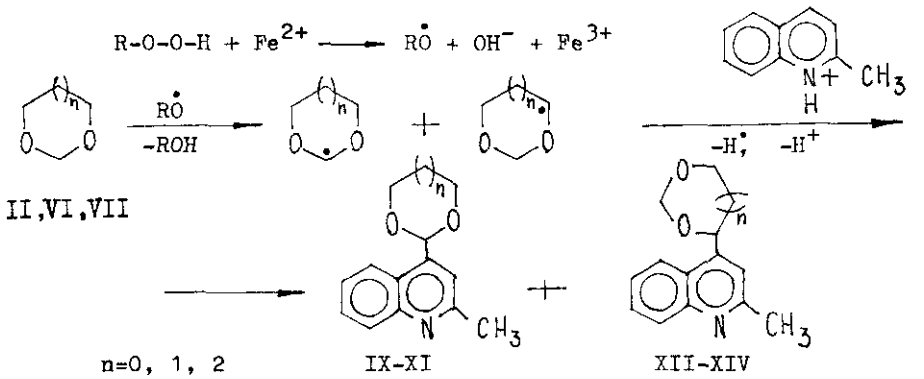
Abstract——— *Homolytical reaction between protonated bases and 1,3-diheterocycloalkanes was described.*

Alkoxylic radicals are known to react with 1,3-oxaheterocycloalkanes and attack preferably methylene or methenyl groups adjacent to two heteroatoms[1-3]. *In this* connection we describe unexpected and surprising data of the work[4], in which the main product of alkylation initiated by $(CH_3)_3C$-O-O-H+$FeSO_4$ system of protonated quinoxaline (I) with 1,3-dioxolane (II) is 2-(1,3-dioxolane-4-yl)quinoxaline (III) but not isomeric 2-(1,3-dioxolan-2-yl)quinoxaline(IV).

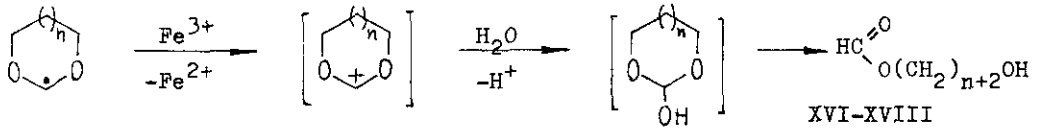

III


IV

We repeated this experiment using a system of R-O-O-H+$FeSO_4$(R=$(CH_3)_3C$;$C_6H_5(CH_3)_2C$) as initiator and found out that product (IV) is formed more selectively than isomeric substances (III)(Table I). Then we drew some 1,3-oxaheterocycloalkanes (II, VI-VIII) into homolytical alkylation of protonated 2-methylquinoline (V) using a system of R-O-O-H+$FeSO_4$(R=H;$C_6H_5(CH_3)_2C$) as donor of alkoxylic radicals. In this case of compounds (II,VI,VII) we established parallel formation of 2- and 4-substituted 1,3-dioxacycloalkanes (IX-XIV), whereas oxathiocyclane (VIII) gave 2-substituted product (XV) only.



We found out that selectivity of products (IX,XII) formation from 1,3-dioxolane (II) depends on initiator nature (Table I). Under the influence of hydroxyl radicals (system H_2O_2+$FeSO_4$) 2- and 4-substituted products (IX,XII) are formed in equal amount whereas 4-(1,3-dioxolan-2-yl)-quinaldine (IX) is formed six times as much as its isomer (XII) under the influence of $C_6H_5C(CH_3)_2\dot{O}$ radicals. At the same time the type of initiator does not influence the selectivity of formation of products from acetals VI and VII. We think that the difference in strength of C^2-H and C^4-H bonds in reaction with $\dot{O}H$ and $C_6H_5C(CH_3)_2\dot{O}$ radicals practically does not exist. Simulteneously with the joining to aromatic system cyclic dialkoxyalkyl radicals react with ions Fe^{+3} resulting in formation of the corresponding carbocations which form in aqueous medium at first unstable 2-oxy-1,3-dioxacyclanes and then monoformates of glycols XVI-XVIII. The rate of this reaction considerably depends on the cycle range in dialkoxyalkyl radicals; for example: oxidation of six- and seven-membered radicals proceeds much more rapidly than of 1,3-dioxolane-2-yl radicals[5-6]. This fact is supposed to explain the decrease of selectivity of formation of X and XI in comparison with IX and XIV.

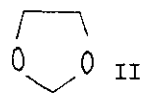
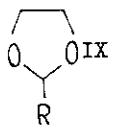
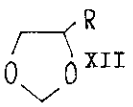
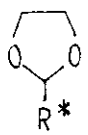
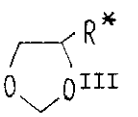
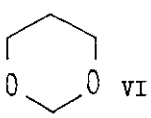
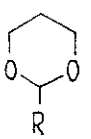
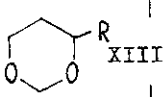
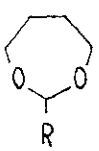
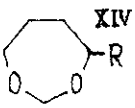
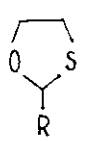


XVI-XVIII

During this reaction monoformates of the corresponding diols (XVI-XVIII) are formed as accessory products. Reaction of protonated base with acetals (II,VI-VIII) was carried out in glass reactor under the following conditions: concentrated aqueous solution of $FeSO_4$(0.06mol) and 30% solution of hydrogen peroxide (H_2O_2) or cumul hydroperoxide ($C_6H_5C(CH_3)_2OOH$)(0.06mol) were added for 30 min intensively stirring at 5-10°C to the reaction mixture and pH 4~5. The reaction mixture contained 0.04 mol of the base (I,V) protonated by sulfuric acid and 0.02 mol of 1,3-diheterocycloalkane (II,VI-VIII); both were dissolved in 50 ml of water. The pH of mixture was maintained at level 4-5 by concentrated Na_2CO_3 solution. After the synthesis was finished pH of the solution was increased to level 12-13 by means of addition of NH_4OH solution and was extracted by ether. Ethereal extracts were joined together and vapored; products were isolated by column liquid chromatography method (Al_2O_3,eluent,mixture of petrolein ether and diethyl ether in ratio 3.5:1).

TABLE I

The Yield of Hydrogen Atom Substitution Products in Quinaldine and Benzpyrazine on 1,3-Oxaheterocycloalkyl Residue at 5-10°; pH=4-5; reaction time 30 min

Acetals	Products	Yield of the reacted base, %	
		$H_2O_2+Fe^{2+}$	$C_6H_5C(CH_3)_2OOH + Fe^{2+}$
 II	 IX	35	76
	 XII	35	14
	 IV	-	71
	 III	-	8
 VI	 X	8	7
	 XIII	22	24
 VII	 XI	2	3
	 XIV	31	30
 VIII	 XV	-	90

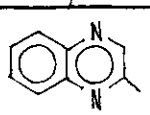
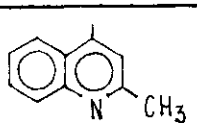
Where R* =  R = 

TABLE II

Reaction Products Spectral Data and Physico-Chemical Constants

Compounds	n_D^{20} t°melt. °C	PMR				NMR			
		Acetals		Quinaldine		Acetals		Quinaldine	
		C^2-H	C^4-H,C^5-H, C^6-H,C^7-H	Me	Ar	C^2	C^4,C^5,C^6, C^7	Me	Ar
IX 4-(1,3-Dioxolan-2-yl)-quinaldine	1.6058	6.15s	3.86s	2.58s	7.0-8.0s	100.7d	65.2t	25.0q	118.2-158.5m
XII 4-(1,3-Dioxolan-4-yl)-quinaldine	1.5875	5.03d	4.10-4.70m 5.33t	2.58s	7.20-8.03m	96.0t	71.3t 74.3d	25.9q	117.7-158.3m
X 4-(1,3-Dioxane-2-yl)-quinaldine	-	5.62s	1.57-1.80m 3.75-4.05m	2.55s	7.10-7.93m	99.4d	32.4t 67.7t	26.6q	119.3-158.3m
XIII 4-(1,3-Dioxan-4-yl)-quinaldine	-	4.84d	1.75-2.00m 3.63-4.22m 4.87d	2.55s	7.08-8.00m	94.4t	34.4t 66.9t 74.4d	26.0q	118.5-158.7m
XI 4-(1,3-Dioxypan-2-yl)-quinaldine	-	6.00s	1.28-1.90m 5.67-4.00m	2.60s	7.05-8.05m	98.9d	26.2t 66.4t	25.1q	123.0-158.7m
XIV 4-(1,3-Dioxypan-4-yl)-quinaldine	-	4.80d	1.30-1.91m 5.20d	2.60s	7.10-8.03m	93.7d	28.9t 36.7t 67.4t 75.2d	25.1q	118.1-158.3m
XV 4-(1,3-Oxathiolane-2-yl)-quinaldine	74	6.36s	2.81-3.17m 3.70-4.00m 4.23-4.55m	2.62s	7.06-8.05m	83.2d	34.4t 72.5t	25.8q	117.6-159.1m

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