Nucleophilic Character of Acyl Radicals. Homolytic Acylation of Quinoxaline

By G. P. Gardini * and F. Minisci, Istituto di Chimica Organica, Università di Parma, 43100 Parma, Italy

The reaction of quinoxaline with aldehydes in the presence of a redox system has been developed as a route to alkyl and aryl quinoxalin-2-yl ketones.

A NEW type of aromatic substitution was reported by us in a preliminary note; [1] it involves homolytic acylation by means of acyl radicals obtained from oxidation of aldehydes.

Heterocyclic bases are especially suitable for this reaction, because (*a*) the acylation can be carried out on aqueous solutions of the corresponding salts, in which the nucleophilic reactivity of the acyl radicals with respect to the substrate is increased, and (*b*) the usual electrophilic aromatic substitution conditions do not usually work for heterocyclic bases and, in any case, would yield substituent orientations different from those found in homolytic acylation, which is highly selective for positions of strong nucleophilic reactivity.

We now report that aldehydes widely different in structure can be used as acylating precursors. Quinoxaline was used as a substrate for this study in order to make the isolation and analysis of the products easier, since it can only give one monoacyl derivative.

The results from the reactions with a variety of aldehydes are shown in the Table. The great reactivity of quinoxaline towards acyl radicals is shown by the success of the reaction with the pivaloyl radical, which usually undergoes rapid competitive decarbonylation.[2]

2-Acylquinoxalines obtained by the reaction of aldehydes (RCHO) with quinoxaline

R	Procedure	M.p.	Yield * (%)	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N
Me	*a*	76—77°†	70				$C_{10}H_8N_2O$			
Et	*a*	104—105	73	70·95	5·75	14·9	$C_{11}H_{10}N_2O$	70·95	5·41	15·05
Pr^i	*a*	55—56	46 ‡	72·0	6·05	13·7	$C_{12}H_{12}N_2O$	71·97	6·04	13·99
Bu^t	*a*	75—76	62 §	72·6	6·4	13·35	$C_{13}H_{14}N_2O$	72·87	6·59	13·08
CH_3·CH:CH	*a*	105	45	72·8	5·25	14·05	$C_{12}H_{10}N_2O$	72·71	5·08	14·13
2-Furyl	*a*	124—125	51	69·7	3·75	12·5	$C_{13}H_8N_2O_2$	69·63	3·60	12·50
Ph	*b*	80—81 ¶	55				$C_{15}H_{10}N_2O$			
p-MeO·C_6H_4	*b*	113	53	72·85	4·45	10·7	$C_{16}H_{12}N_2O_2$	72·71	4·58	10·60
3,4-$(MeO)_2C_6H_3$	*b*	124	54	69·1	4·9	9·4	$C_{17}H_{14}N_2O_3$	69·28	4·79	9·52
p-ClC_6H_4	*b*	105	52	66·75	3·4	10·25	$C_{15}H_9ClN_2O$	67·05	3·38	10·43

* Based on initial quinoxaline; yields based on actually converted quinoxaline were practically quantitative. † Lit.,[2] 77°. ‡ Less than 10% of alkylated products were found. § Less than 5% of alkylated products were found. ¶ Lit.,[3] 80—81°.

EXPERIMENTAL

Unless otherwise stated, i.r. spectra were measured as for potassium bromide discs, u.v. spectra for solutions in methanol, and 60 MHz n.m.r. spectra for solutions in deuteriochloroform (tetramethylsilane as internal reference). G.l.c. analyses were performed with a Varian Aerograph 1200 flame ionisation chromatograph, with a column containing SE30 (5%) and dimethylchlorosilane supported on Chromosorb W.

General Procedures for Acylation of Quinoxaline.—(*a*) Saturated solutions of iron(II) sulphate (0·06 mole) and t-butyl hydroperoxide (0·06 mole) were added dropwise simultaneously to a stirred and cooled (5—15°) mixture of aldehyde (0·06 mole), quinoxaline (0·02 mole), and 4M-sulphuric acid (0·02 mole). The mixture was then stirred for a further 10 min., neutralised with sodium hydrogen carbonate and extracted with ether (the product may be insoluble in the reaction medium and can be collected by direct filtration: this was the case with the prop-1-enyl and 2-furyl ketones). G.l.c. analysis of the ether extract showed that the expected product was the only quinoxaline derivative formed. Some alkylated products were found in the reactions with isobutyraldehyde and pivalaldehyde.

(*b*) The conditions were essentially the same as in (*a*), but acetic acid (20—40 ml.) was added in order to bring the aldehyde into solution. Again precipitation of the product may occur spontaneously or upon addition of water.

The methyl [3] and the phenyl [4] quinoxalin-2-yl ketones have been described in the literature. Our products were identical with those synthesised by the reported procedure. U.v., i.r., n.m.r., and mass spectra were consistent with the expected structures for all compounds.

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