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IPSO-SUBSTITUTIONS. REACTIONS OF 3-SUBSTITUTED INDOLES WITH BENZOYLPEROXIDE

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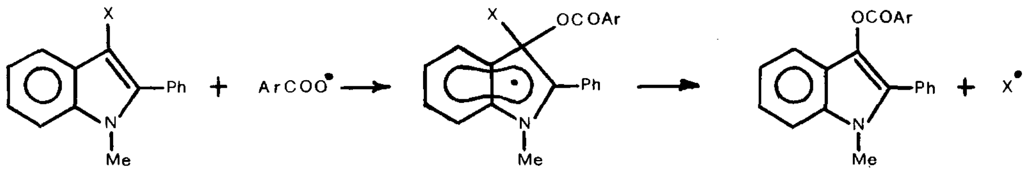
Summary: 3-substituted indoles with benzoylperoxide led to the 3-benzoyloxy derivative.The reaction is discussed in terms of homolytic ipso-substitution.

Recently we observed that nitronium and nitrosonium ions[1] reacted with 3-substituted indoles to form 3-nitroindole. In this letter we report the results for the reaction between 3-substituted indoles and benzoylperoxide. In this case also the benzoyloxy group displaces the substituent at C-3 to form the 3-benzoyloxy derivative 3a (Scheme 1). All reactions were carried out at room temperature in benzene or pyridine and in every case compounds 3a and unchanged starting materials were the only compounds isolated.

Scheme 1



1 2 3a,b

X=H; CH_2OH; CH_2-(3'-indolyl); CH(Ph)-(3'-indolyl); N_2Ph; $COCH_3$; CHO. a:Ar=Ph; b:Ar=p-MeO-C_6H_4-

Indipendently from the mechanism involved in the reaction pathway, on the basis of the reaction time and the yield of compound 3a, we can hypothesize that the ipso-substitution for the studied groups follows the sequence:

H $\geqslant$ CH_2OH $>$ CH_2-(3'-indolyl) $\geqslant$ CH(Ph)-(3'-indolyl) $>$ N_2Ph $>$ $COCH_3$ $\geqslant$ CHO, which is the same as that we proposed for the reactions with nitronium ion.[1] The reaction between unsubstituted indoles and benzoylperoxide has already been studied by others,[2] but the mechanism was discussed either in terms of homolytic or heterolytic factors.

It is well known that the acylperoxides undergo a homolytic decomposition in the presence of amines.[3,4,5] Therefore we thought the reactions described herein and carried out in pyridine, which are faster than those carried out in benzene (see Table), might take place through a homolytic ipso-substitution. In fact, if the reaction between 1-methyl-2-phenylindole or 1-methyl-2-phenyl-3-hydroxymethylindole and benzoylperoxide was performed in pyridine in the presence of a a large excess of p-methoxybenzoic acid, compound 3a was isolated together with a small amount

Table. Reactions times and % yields of 3a

1	Solvent	Time(hrs)	3a(% yield)
X = H	a	120	50
	b	24	50
X = CH_2OH	a	120	32
	b	24	49
X = $-CH_2-$ -(3'-indolyl)	a	120	24
	b	48	40
X = -CH(Ph)- -(3'-indolyl)	a	120	25
	b	24	25
X = N_2Ph	a	120	16
	b	70	24
X = $COCH_3$	a	120	0
	b	120	10
X = CHO	a	120	0
	b	120	7

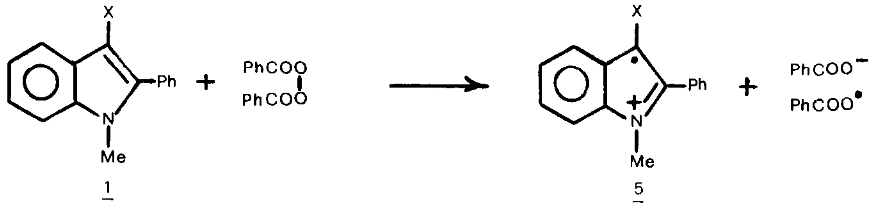
a, benzene; b, pyridine.

of 1-methyl-2-phenyl-3-(p-methoxybenzoyloxyl)-indole 3b. The formation of the latter compound could be explained by assuming the presence of p-methoxybenzoyloxyl radical in the reaction medium and the equilibrium:[6]

$$PhCOO^{\bullet} + p\text{-}MeO\text{-}C_6H_4\text{-}COOH \rightleftharpoons p\text{-}MeO\text{-}C_6H_4\text{-}COO^{\bullet} + PhCOOH$$

As to the reactions performed in benzene, the mechanism could also involve homolytic decomposition of the benzoylperoxide, but, in this case, the O-O bond cleavage would be induced by the indole nucleus. Thus the operant mechanism would be that shown in Scheme 2.

Scheme 2



This supposition was confirmed by the experimental results. In fact, indoles bearing substituents at C-3 like $COCH_3$ or CHO, which increase the oxidation potential of the indole nucleus, do not undergo the electron transfer process shown in Scheme 2 and do not react at all.

Compound 3a: m.p. 101°(benzene/petroleum ether); I.R., 1725 cm^{-1} (C=O); ^1H N.M.R., in $CDCl_3$(int. TMS): 3.72(3H, s, CH_3); 7.0--7.7(12H, m, arom.); 8.12-8.38(2H, m, arom.). Anal. Found: C,80.90; H,5.29; N,4.03. Calcd. for $C_{22}H_{17}NO_2$: C,80.71; H,5.23; N,4.28.

Compound 3b: I.R. 1730 cm^{-1}(C=O); ^1H N.M.R., in $CDCl_3$(int. TMS): 3.72(3H, s, NCH_3); 3.89(3H, s, OCH_3); 7.0-7.8(11 H, m, arom.); 8.12-8.40(2H, m, arom.). M^+, Found: 357; calcd. for $C_{23}H_{19}NO_3$: 357,41.

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