OXIDATION OF PYRROLES WITH BENZOYL PEROXIDE[1]

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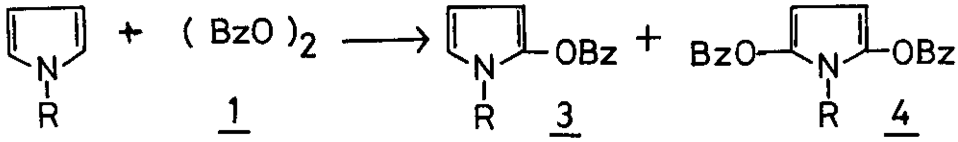
Upon treatment with benzoyl peroxide 1, N-substituted pyrroles 2 afforded 2-benzoyloxy- 3 and 2,5-dibenzoyloxypyrroles 4. N-Substituted pyrrole-2-carbinols 5 undergo novel C-C cleavage with 1 to also give 3 and 4.

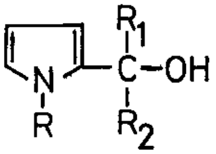
Although homolytic substitution of aromatics with benzoyl peroxide 1 has been studied extensively,[2,3] relatively little attention has been directed to that of heterocycles.[3,4] It has been known that thiophene and furan, upon treatment with 1, form 2- and 3-phenylthiophene,[5] and 2,5-dibenzoyloxydihydrofuran,[6] respectively. We have recently reported that 1 converts N-methylindole into indoxyl, oxindole and dioxindole O-benzoates.[7]

Reaction of pyrrole with 1 was difficult to control giving intractable tar. However, N-substituted pyrroles 2a – d were moderately reactive toward 1 giving



a : R = CH_3 ; b : R = $C_6H_5CH_2$; c : R = C_6H_5 ; d : R = p-$CH_3OC_6H_4$

Scheme 1



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a : $R = CH_3$, $R_1 = R_2 = H$
b : $R = CH_3$, $R_1 = H$, $R_2 = C_6H_5$
c : $R = CH_3$, $R_1 = R_2 = C_6H_5$
d : $R = C_6H_5$, $R_1 = R_2 = H$

Table Yields (%) of Benzoyloxypyrroles[†]

substrate		2a	5a	5b	5c		2b		2c[‡]	5d		2d
product	3a	27	7	28	–	3b	24	3c	18	19	3d	28
	4a	30	27	42	56	4b	35	4c	10	24	4d	8

[†] Unless otherwise stated, a benzene solution containing an equimolar amount of 1 and a pyrrole derivative was reacted : 2a, at room temp. for 24 hr; 5, at room temp. for 1 hr; 2b, 60° for 2 hr; 2d, 60° for 24 hr.

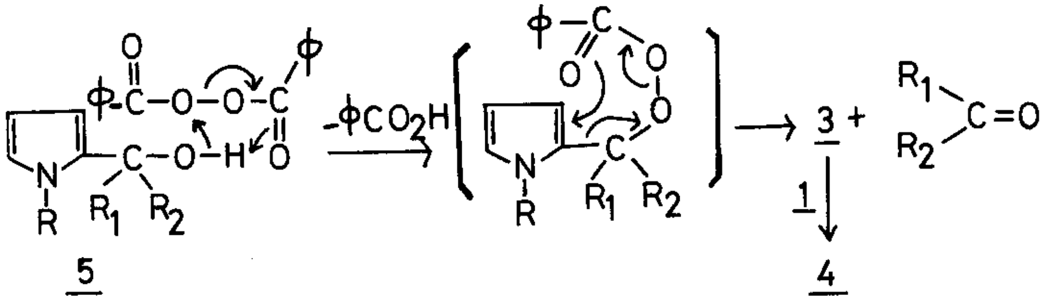
[‡] An acetonitrile solution was refluxed for 24 hr.

both 2-benzoyloxypyrroles 3a – d[8] and 2,5-dibenzoyloxypyrroles 4a – d[8] (Scheme 1). The results are listed in the table. Neither 3-benzoyloxy nor phenylated products were isolated. N-Phenylpyrrole 2c was less reactive than the N-alkyl analogs 2a – b, while this effect was somewhat compensated by the p-methoxy group in 2d, clearly indicative of the polar effect on this reaction. Since the benzoyloxy radical is known to be electrophilic,[1,2,7,9] this oxygenation must be associated with the strong nucleophilic character of the pyrrole ring. A plausible mechanism may involve an induced decomposition of 1[5] followed by an electrophilic attack on the pyrrole ring by the benzoyloxy radical.[7]

A comparison of the reactivities of thiophene, furan and pyrrole, the fundamental heteroaromatic series, is now available in terms of their behavior towards 1.[10] The reactive order is pyrrole > furan > thiophene, consistent with other studies of their homolytic reactions.[11] That thiophene is least reactive is indicated by the observation that only the phenylated products were obtained.[5-7] The contrasting behavior of furan and pyrroles towards 1 is rationalized by considering the greater aromaticity of the pyrrole ring than furan.[12]

In addition, these products (3 and 4) are found to be interesting synthetic substrates, for example, in the Diels-Alder reaction, due to activation of the pyrrole ring by the benzoyloxy substituent. This synthetic application will be reported separately.

In the course of this study, it was observed that N-methyl-pyrrole-2-carbinol 5a, on treatment with 1, undergoes facile cleavage of the carbon-carbon bond giving rise to the benzoyloxy derivatives (3a and 4a).[8] Under the mild conditions, 5b - d were similarly transformed into the mono and/or dibenzoyloxy derivatives demonstrating the generality of this reaction (table). Benzaldehyde was identified as the counterpart of the fragmentation in the case of 5b. This unusual oxidative transformation, probably analogous to the fission of methyl-t-butylcarbinol with lead tetraacetate,[13] may be characteristic of the pyrrole ring since, for example, furan-2-carbinol did not react under similar conditions. The mechanism, though unknown yet, could be tentatively explained by involvment of ionic cleavage of an intermediate perbenzoate (Scheme 2).



Scheme 2

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