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FLASH VACUUM PYROLYSIS OF 2-BENZYLPYRIDINE *N*-OXIDES. SYNTHESIS OF METHYLPYRIDO[1,2-*a*]INDOLES

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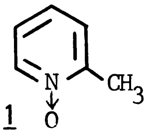
Flash vacuum pyrolysis of 2-benzylpyridine *N*-oxides afforded pyrido[1,2-*a*]indole and its various methyl-substituted derivatives in moderate yields. Benzo[*g*]quinoline in the pyrolyses of 2-(*o*-methylbenzyl)pyridine *N*-oxide and 2-benzyl-3-methylpyridine *N*-oxide, and 2-(β-styryl)pyridine in the reaction of 2-(β-phenethyl)pyridine *N*-oxide were major products as exceptional cases.

We have reported[1)] that the flash vacuum pyrolysis[2)] (FVP) of 2-picoline *N*-oxide (**1**) gave products derived from the intermediary 2-picolyl (2-pyridylmethyl) radical (**2**).

We now wish to report an application of phenyl(2-pyridyl)methyl radicals (**3**), which are formed from 2-benzylpyridine *N*-oxides (**4**) through the FVP, to the synthesis of methylpyrido[1,2-*a*]indoles (**5**).

As a preliminary experiment, 2-ethylpyridine *N*-oxide was pyrolysed[1)] at 800°C (quartz tube, ϕ=10 mm, *l*=150 mm) under 0.1 mmHg. Vinylpyridine was obtained (45%), suggesting the existence of the radical **6** in the reaction course.



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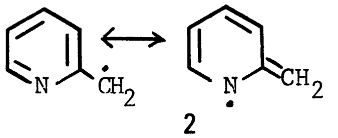

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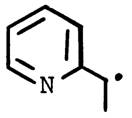

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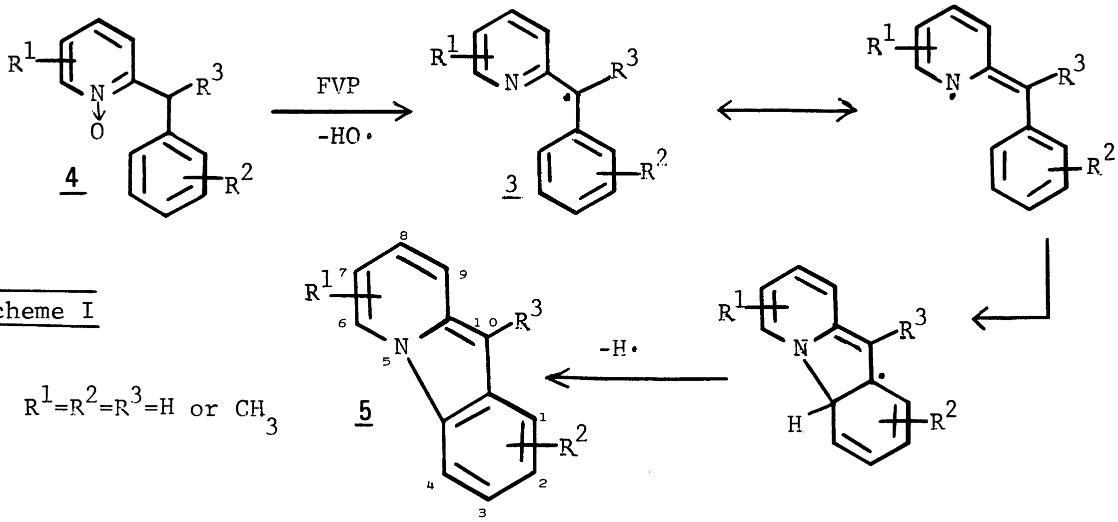
Similarly, the *N*-oxides **4** were pyrolysed (800°C, 0.1 mmHg). An intramolecular cyclization of the radical **3** took place to give pyrido[1,2-*a*]indoles (**5**) as shown in Scheme I (Table I).



Scheme I

$R^1=R^2=R^3=H$ or CH_3

The starting materials were almost completely decomposed under the described conditions, and column chromatography (hexane/alumina) and recrystallizations from pentane or hexane were employed for the isolation of these products. All these pyridoindoles were appreciably unstable.

Table I. FVP of 2-Benzylpyridine N-Oxides (**4**)

4			5^{a}			
R^1	R^2	R^3	R^1, R^2, R^3	Mp, °C	Yields, %	Other Products(%)^{a}
H	H	H	H	175 (lit.^{b} 174)	74	
H	p-CH_3	H	3-CH_3	138	69	
H	m-CH_3	H	2-CH_3^{c}	108	25	
			4-CH_3^{c}	(-)	16	
H	o-CH_3	H	1-CH_3^{d}	(-)	trace	7 (47)
6-CH_3	H	H	6-CH_3	59	42	
5-CH_3	H	H	7-CH_3	138	43	
4-CH_3	H	H	8-CH_3	152	51	
3-CH_3	H	H	9-CH_3	103	10	7 (52)
H	H	CH_3	10-CH_3	69 (lit.^{e} 69)	13	8 (41)

[a] All isolated products have satisfactory analytical and spectral data.

[b] Physical data of the compound were fully identical with those of pyrido[1,2-a]indole; Y. Arata, T. Ohashi, and K. Uwai, Yakugaku Zasshi, 1955, 75, 265.

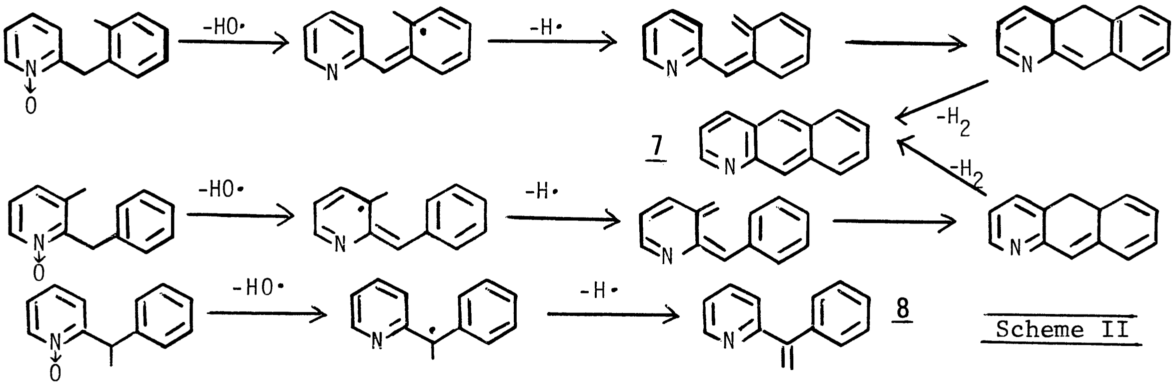
[c] Although NMR and TLC of the crude products showed the presence of 4-methyl derivative, isolation of the product was difficult (the yield was determined by NMR). 2-Methyl derivative was readily isolated.

[d] Isolation of 1-methylpyrido[1,2-a]indole was failed, although NMR and TLC of the reaction mixture suggested the presence of the compound in the mixture.

[e] Physical data of the compound was fully identical with those reported for 10-methylpyrido[1,2-a]indole; R. Robinson and J. E. Saxton, J. Chem. Soc., 1952, 976; H. H. Wasserman and W. R. Waterfield, Chem. and Ind., 1961, 1220.

Thus, the described FVP of 2-benzylpyridine N-oxides was found to be practical for the synthesis of new methylpyrido[1,2-a]indoles.[3]

In some cases, methyl groups of the intermediary radicals participated in liberation of a hydrogen; and benzo[g]quinoline (7) was a major product in the FVP of 2-(o-methylbenzo)pyridine N-oxide and 2-benzyl-3-methylpyridine N-oxide, and an olefin 8 was a major product in the FVP of 2-(β-phenethyl)pyridine N-oxide (Scheme II).



Scheme II

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References

1) A. Ohsawa, T. Kawaguchi, and H. Igeta, Chem. Pharm. Bull.(Tokyo), 1981, 29, 1481.
2) R. F. Brown, "Pyrolytic Methods in Organic Chemistry," Academic Press, N.Y. 1980.
3) Although some syntheses of pyrido[1,2-a]indoles have been known, reported yields are usually low; for the syntheses of the unsubstituted compound, see ref. b in Table I; for the 10-methyl derivative, see ref. e in Table I.

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