

CXLIV.—*Dealkylation of Phenolic Ethers by Pyridine and Piperidine.*

By ROBERT SIDNEY CAHN.

It was found (this vol., p. 630) that the methyl ether of trinitrocannabinol, to which the structure of a polynitrophenol was assigned, was dealkylated by heating for a few minutes with pyridine containing a little water or with piperidine. The result of the application of this reaction to a number of phenolic ethers is shown in the table below. The pyridine used was B.D.H. "pure" pyridine, which contained a little water; addition of a further 25% of water retarded the hydrolysis. Unless otherwise stated, the ethers were heated for one hour with excess of base under reflux, the reaction products being isolated in the usual way. No great accuracy is claimed for estimates of hydrolysis other than nil and 100%.

No.	Ether.	% Hydrolysis to phenol with	
		pyridine.	piperidine.
1	Codeine	nil	—
2	<i>o</i> -Nitroanisole	? slight	ca. 40%
3	<i>m</i> - " "	nil	nil
4	<i>p</i> - " "	nil	very slight
5	2 : 4-Dinitroanisole	ca. 70%	(gave quantitatively 2 : 4-dinitrophenylpiperidine within 15 minutes on the water-bath)
6	3 : 5-Dinitroanisole	nil	mostly unchanged after 30 mins. (reflux); resinified on longer heating
7	2 : 4-Dinitrodiphenyl ether	nil	* (rapid reaction on the water-bath to give 2 : 4-dinitrophenylpiperidine and phenol)
8	2 : 4 : 6-Trinitroanisole	100% in 1 min.	100% in 1 min.
9	3-Nitro- <i>p</i> -tolyl methyl ether (I)	slight	ca. 20%
10	5-Nitro- <i>o</i> -tolyl methyl ether (II)	100% (50% after 45 mins. on the water-bath)	almost 100%
11	6-Methoxy- <i>m</i> -toluic acid	nil	—
12	5-Nitro-6-methoxy- <i>m</i> -toluic acid	nil	—
13	2 : 4 : 6-Trichloroanisole	nil	—

* Le Fèvre, Saunders, and Turner, *J.*, 1927, 1168.

It thus appears that the rate of hydrolysis of these ethers, though partly dependent on the acidity of the phenol, is influenced not only by the nature but also by the position of the substituents. This is clearly shown by the contrast between the isomeric pairs of ethers 5 and 6, and 9 and 10, but the complicated nature of the influences

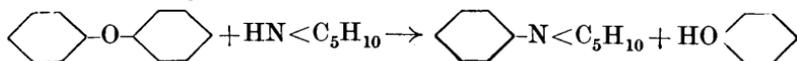


at work is indicated by the fact that the rate of hydrolysis of *p*-nitroanisole by piperidine is very greatly increased by the introduction of a methyl group into the nucleus (ethers 4 and 10), and that of *o*-nitroanisole somewhat decreased (compare Schorigin, Issaguljanz, and Below, *Ber.*, 1931, 64, 274, who record the varying effect of the same substituents in different positions upon the hydrolysis of phenolic ethers by water under pressure).

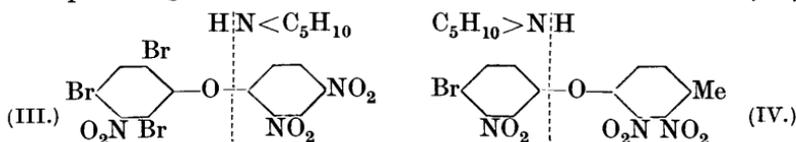
Most remarkable is the fission of 2 : 4-dinitroanisole by piperidine ; this ether is the only anisole examined which resembles the diphenyl ethers in yielding a phenylpiperidine derivative.* In this connexion it should be noted that mononitrodiphenyl ethers appear to be unaffected by piperidine (Le Fèvre, Saunders, and Turner, *loc. cit.*)

* A special experiment and many of Turner's results showed that dinitrophenylpiperidine is a primary product of the reaction, as it is not formed by heating dinitrophenol and piperidine under reflux.

and that 2 : 4 : 6-trinitrophenyl *p*-tolyl ether gives 2 : 4 : 6-trinitrophenylpiperidine and *p*-cresol (Reilly, Drumm, and Gray, *Sci. Proc. Roy. Dublin Soc.*, 1930, **19**, 461). Turner and his collaborators (*loc. cit.* and later papers) have shown that the fission of diphenyl ethers according to the scheme

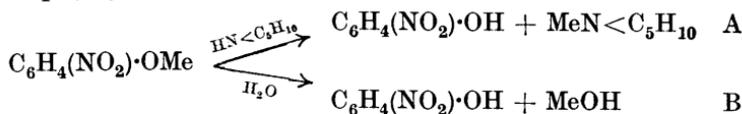


proceeds in general in such a way that the more negatively substituted phenyl group becomes attached to the piperidine residue, but there are indications that this regularity does not always hold. This is clearly shown by (*inter alia*) the ethers (III) and (IV), which are split along the dotted lines marked (Miss Fox and Turner, J.,



1930, 1853), though it is not clear whether the difference in this case is due to the methyl group or to the 3'-nitro-group being in the meta-position relative to the ether group or to both effects. The results obtained with the anisoles lead to the expectation that investigation of suitable diphenyl ethers will disclose further irregularities.

This method of dealkylation may prove useful, particularly for phenols or ethers which are unstable to caustic alkalis (*e.g.*, trinitrocannabinol methyl ether) or to mineral acids, but a detailed study will be necessary to enable its applicability to be forecast or theoretical conclusions to be drawn from its variability. It has not, *inter alia*, been determined whether fission of *o*-nitroanisole (for example) by piperidine proceeds according to scheme A or B :



The ethers 3, 4, 5 and 8 were prepared for this investigation in excellent yields by adding the nitrophenol with cooling to excess of a mixture of methyl iodide and freshly precipitated dry silver oxide and keeping the whole at room temperature for 2 hours. This method is more convenient than that involving isolation of the silver salt.

The author is indebted to Professor J. L. Simonsen, Dr. H. R. Ing, and Mr. W. O. Jones for some of the chemicals used in this investigation.