Tetrahedron Letters,Vol.30,No.22,pp 2927-2928,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

ELECTRON-TRANSFER ACTIVATION. PHOTOCHEMICAL N-DEMETHYLATION OF TERTIARY AMINES

J. SANTAMARIA, R. OUCHABANE and J. RIGAUDY

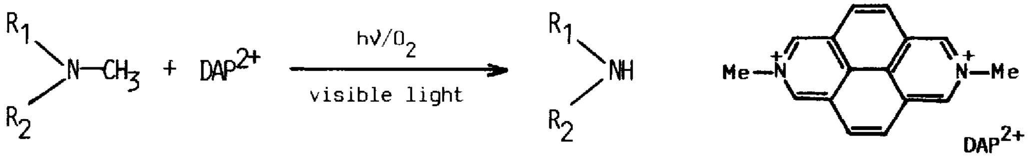
Laboratoire de Recherches Organiques, associé au CNRS (UA 476)
Ecole Supérieure de Physique et Chimie Industrielles
10 rue Vauquelin - 75231 PARIS Cedex 05.

Abstract: DAP^{2+} sensitized photooxidation of some biologically active N-methylated alkaloids affords the corresponding secondary amines in excellent yields (80-95 %).

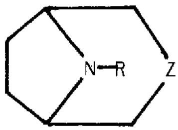
N-Demethylation of tertiary amines can be carried out chemically with chloroformate reagents, which have replaced the older procedure using cyanogen bromide, based on the classical von Braun reaction[1]. Although these methods may be in some cases efficient, the yields are generally limited and toxicity of the required reagents is a real drawback.

During the course of our studies on electron transfer photooxidations, we have found a mild and useful photochemical method for N-demethylation of some alkaloids which can lead to important intermediates for the preparation of biologically active analogues.

A typical procedure is as follows: a solution of the tertiary amine (2 mmol) and a catalytic amount of DAP^{2+}, 2 BF_4^-(0.02 mmol) in acetonitrile (50 ml) is irradiated under oxygen bubbling for 30-120 minutes with a 500 W high-pressure Hg lamp through a U.V. cut-off glass filter (λ⩾ 400 nm) at 20°C. After reaction (followed by t.l.c.) the secondary amine is separated by flash chromatography on alumina. Excellent yields are obtained far better than those afforded by chemical methods (see Table 1).



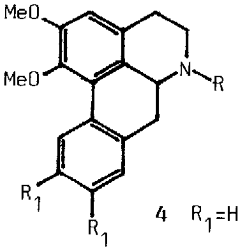
The dication DAP^{2+} (=N,N'-dimethyl-2,7-diazapyrenium)[2] is an electron acceptor which can be excited by visible light, not absorbed by amines. It has been used previously by Lehn for an efficient photocleavage of DNA[3]. The mechanism of the photooxidation is expected to be similar to those suggested when other potential acceptors such as ketones, metal complexes, hydrocarbons or dyes were used. It should imply an electron abstraction from the N lone pair followed by oxidation to an immonium ion which leads by hydrolysis to the secondary amine and aldehyde[4-6].



1 $Z = \mathrm{C}\begin{smallmatrix}H\\OH\end{smallmatrix}$

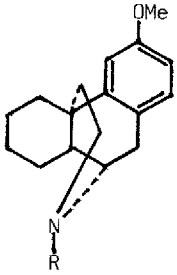
2 $Z = C{=}O$

3 $Z = \mathrm{C}\begin{smallmatrix}H\\OCOCHPhCH_2OH\end{smallmatrix}$



4 $R_1{=}H$

5 $R_1{=}OCH_3$



6

a, $R{=}CH_3$; b, R=H

Table 1. DAP^{2+}-sensitized photooxidation of various tertiary methylated amines.

Amine		Nor-compound[a]	Yields (%)	Notes
Tropine	**1a**	**1b**	87[b]	*a. Nor-compounds have been identified by comparison with authentic samples.* *b. Using Methylene blue leads to a 5% yield[7]. Poor yields were obtained with $KMnO_4$[8], $K_3[Fe(CN)_6]$[9], BrCN[10] or ethyl chloroformate (16%)[11].* *c. The analogue glaucine **5a** suffers only ring fission when treated with α-chloroethyl chloroformate[12].*
Tropinone	**2a**	**2b**	93	
Atropine	**3a**	**3b**	95	
Nuciferine	**4a**	**4b**	65[c]	
Dextromethorphan	**6a**	**6b**[13]	95	

Work is currently underway to explore the mechanism and the generality of this reaction.

Acknowledgments. J.S. thanks Prof. Cavé for the gift of nuciferine and nornuciferine.

REFERENCES AND NOTES

1. J.H. Cooley and E.J. Evain, Synthesis, 1 (1989).
2. DAP^{2+}, 2 BF_4^- was obtained as described in S. Hünig, J. Gross, E.F. Lier and, H. Quast, Liebigs Ann. Chem., 339 (1973).
3. A.J. Blacker, J. Jazwinski, and J. M. Lehn, Helv. Chim. Acta, **70**, 1 (1987).
4. K. Monserrat, J.K. Foreman, M. Graetzel, and D.G. Whitten, J. Amer. Chem. Soc., **103**, 6667 (1981).
5. D. Döpp and J. Heufer, Tetrahedron Lett., 1553 (1982).
6. A. Ledwith, Acc. Chem. Res., 5, 133 (1972).
7. F. Khuong-Huu, D. Herlem, and Y. Hubert-Brierre, Tetrahedron Lett., 359 (1975).
8. G. Werner, R. Hackel, N. Mohammad, N. Seller, and K.H. Störr, Liebigs Ann. Chem., **708**, 210 (1967).
9. S.P. Findlay, J. Amer. Chem. Soc., **75**, 3204 (1953).
10. A. Nickon and L.F. Fieser, J. Amer. Chem. Soc., **74**, 5566 (1952).
11. G. Kraiss and K. Nador, Tetrahedron Lett., 57 (1971).
12. R.A. Olofson, J.T. Martz, J.P. Senet, M. Piteau, and T. Malfroot, J. Org. Chem., **49**, 2081 (1984).
13. **6b.** m.p. 253 °C ; M^+ 257 (89 %, $C_{17}H_{23}NO$), 212, 136. $[\alpha]_D$ = + 32° (c = 0.5, CH_3OH) ; ^1H NMR ($CDCl_3$, δ) 3.80 (3H, s, OCH_3), 6.96 (3H, m, H arom.), 8.53 (1H, s, broad, D_2O exchangeable NH).
N-acetyl derivative. M^+ 299 (15 %, $C_{19}H_{25}NO_2$), 256, 213 ; $[\alpha]_D$ = + 171° (c = 0.5, CH_3OH) ; IR ($CHCl_3$, cm^{-1}) 1640 (amide C=O) ; ^1H NMR ($CDCl_3$, δ) 2.03 (3H, s, $NCOCH_3$), 3.76 (3H, m, OCH_3) 6.83 (3H, m, H arom.).

(Received in France 6 February 1989)