

ANODIC N-DEARYLATION OF 2-AZETIDINONES

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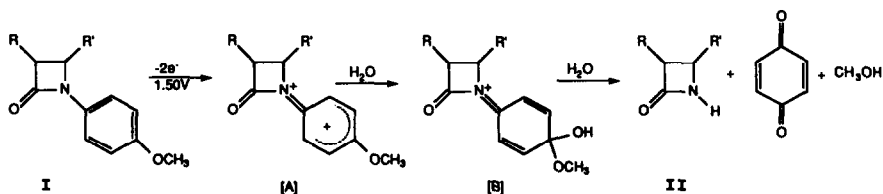
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Abstract: N-Methoxyphenyl-2-azetidinones are dearylated under mild conditions via anodic oxidation.

Several reports have appeared which have discussed the use of p-anisidine as the nitrogen source in the synthesis of 2-azetidinones.^{1,2,3} The p-methoxyphenyl group is then oxidatively cleaved with ceric ammonium nitrate (CAN). We wish to report the electrochemical cleavage of the p-methoxyphenyl moiety via anodic oxidation as an effective alternative to CAN.

The use of CAN, while high yielding in many cases, has some disadvantages associated with its use which become particularly evident when the reaction is run on a large scale. Due to its high equivalent weight (548) and the use of 3 equivalents per mole of substrate, the reaction requires massive quantities of reagent. The use of stoichiometric quantities of CAN is not only uneconomical, but the discarding of the large quantities of spent reagent is a serious environmental obstacle. Attempted use of catalytic CAN with a secondary oxidant was reported to give inferior results.¹

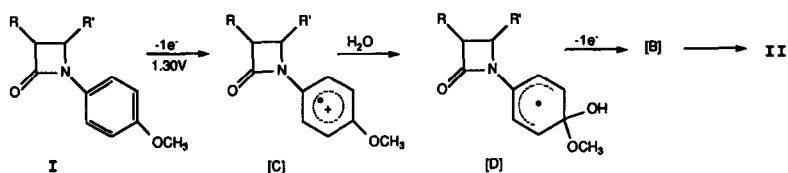
A variety of N-p-methoxyphenyl-2-azetidinones were synthesized by standard methods. Voltamograms of lactams Ia-h exhibited two waves at 1.20-1.30 V and 1.50- 1.60 V corresponding to two one-electron oxidations.⁴ Since the electrolyses were carried out at 1.5 V the reaction most likely proceeds through the di-cation [A] depicted in Scheme 1.



Scheme 1.

This mechanism is consistent with prior reports on the oxidation of p-methoxyanilides.^{5,6}

When the electrolyses were carried out at potentials corresponding to the first wave of the voltamogram (1.2-1.3 V), lower yields of II were obtained with a concomitant increase in by-products. These lower yields may be explained on the basis of alternate



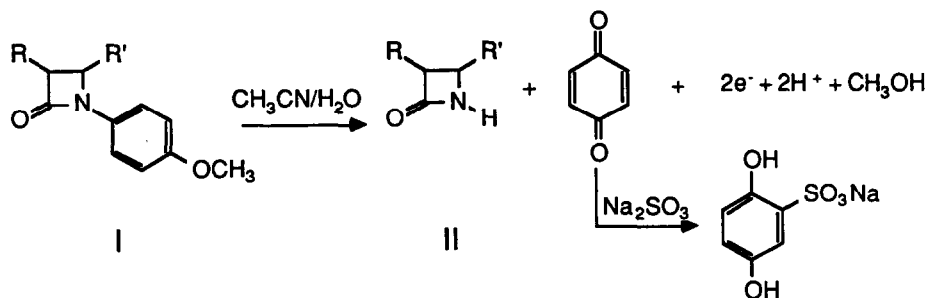
Scheme 2.

degradation pathways for radical-cation **[C]** (Scheme 2) such as dimerization and H atom abstraction.

The results of anodic oxidation of **I** a-h are shown in Table 1. The procedure is simple, and the reaction is mild and selective. Typically, a solution of the azetidinone (**I** a-h) 1 mmol, in 10:1 CH_3CN/H_2O containing 1% $LiClO_4$ as supporting electrolyte, is stirred in an open beaker at ambient temperature. The solution is electrolyzed at 1.50 volts until the current has dropped off to near background levels and the starting material has been consumed.^{7,8,9} After removal of the solvent, the residue is dissolved in ethyl acetate and the benzoquinone by-product is extracted with 10% Na_2SO_3 . The lactam is then isolated either by direct crystallization or by column chromatography.

In conclusion we have reported a mild, selective, "reagentless" method for N-dearylation of 2-azetidinones that does not require highly sophisticated electronic gear and which circumvents all of the difficulties associated with the use of cerium (IV) reagents.

Table I



	<u>R</u>	<u>R'</u>	(Lactam geometry)	<u>Yield II</u>
a)	$-\text{CH}_3$		(cis)	85%
b)	$-\text{N}_3$		(cis)	59%
c)		Ph	(cis)	60%
d)			(cis)	80%
e)			(trans)	80%
f)			(trans)	95%
g)	$-\text{N}_3$		(cis)	66%
h)		CO_2Et	(cis)	60%

References and notes

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2. G.I. Georg, J. Kant, H.S. Gill, J. Amer. Chem. Soc., (1987), 109, 1129.
3. C. Cainelli, DiGiacomini, M. Pananzio, G. Martelli, G. Spunta, Tet. Lett. (1987) 28, 3593.
4. Peak potentials were measured from cyclic voltammetry with a BAS-100 electrochemical analyzer using a glassy carbon working electrode (BAS), a Ag/AgCl reference electrode (BAS) and a platinum wire auxiliary electrode.
5. H. Ohmori, C. Ueda, Y. Nobusue, N. Suitou, T. Yokota, M. Masui, J.C.S. Perkin Trans. II (1974) 1599.
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7. Compound Ib was oxidized at 1.45 volts in a divided cell which was constructed by inserting the cathode into a glass tube with a fritted glass filter at the end and suspending it in the beaker.
8. Compound Ig was oxidized at 1.60 volts in the same divided cell reactor.
9. The anode consisted of a piece of reticulated vitreous carbon (RVC), a "foam" of glassy carbon. The cathode was a stainless steel spatula and the reference electrode was a Ag/AgCl reference electrode (Fisher). A PAR Model 173 potentiostat was the voltage source.

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