Anodic Oxidation of Alicyclic Bromides in Acetonitrile

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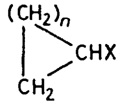
The electro-oxidation of alicyclic bromides in acetonitrile has been investigated. Cycloheptyl, cyclohexyl, and cyclopentyl bromides each gave the corresponding *N*-cycloalkylacetamide and cycloalkene. Cyclobutyl bromide gave only *N*-cyclobutylacetamide whereas cyclopropyl bromide underwent ring-opening and yielded *N*-allylacetamide. The mechanism of formation of the products is discussed and the effect of concentration, temperature, supporting electrolyte, and amount of electricity consumed was studied in the oxidation of bromocyclohexane.

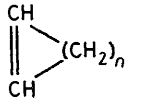
RECENTLY we examined the anodic oxidation of primary, secondary, and tertiary aliphatic bromides, with both straight- and branched-chains.[1,2] All compounds studied showed an exclusive carbon–bromine bond cleavage in acetonitrile, unlike certain bromoadamantyl derivatives which also undergo carbon–hydrogen bond breaking.[3] *N*-Alkylacetamido-derivatives were the sole products isolated from these oxidations.

We have now extended our investigations to electro-oxidation of alicyclic bromides, to study the effect of ring-size on the course of the oxidation.

RESULTS

Bromocycloheptane (I), bromocyclohexane (II), bromocyclopentane (III), bromocyclobutane (IV), and bromocyclopropane (V) were potentiostatically oxidized in acetonitrile using a platinum anode and Ag/0.1M-AgNO$_3$ as a reference electrode. Substrates (I)—(IV) yielded the corresponding *N*-cycloalkylacetamides, (Ia)—(IVa), whereas compound (V) yielded *N*-allylacetamide (Va). Furthermore, the oxidation of (I)—(III) gave also olefins, cycloheptene (Ib), cyclohexene (IIb), and cyclopentene (IIIb) respectively.





	n	X		*n*	X		*n*
(I)	5	Br	(Ia)	5	NHAc	(Ib)	5
(II)	4	Br	(IIa)	4	NHAc	(IIb)	4
(III)	3	Br	(IIIa)	3	NHAc	(IIIb)	3
(IV)	2	Br	(IVa)	2	NHAc		
(V)	1	Br	(Va)	=	CH$_2$:CH·CH$_2$NHAc		

TABLE 1

The effect of temperature on the yield of (IIa) and (IIb) in the anodic oxidation of [(II)] = 0.5M at 2.5 V *vs.* Ag/0.1M-AgNO$_3$ [a]

T/°C	% (IIa)	% (IIb) [b]	Total product yield (%)
22	37	8	48 [c]
0	60	14	74 [d]
−20	50	6	56

[a] In all runs, 0.2M-tetraethylammonium fluoborate (TEAF) was used as an electrolyte. The electrolysis in each experiment was stopped after passing 0.8 F/mol. Yields are based on calibration curves which were previously made for (IIa) and for the 1,2-dibromocyclohexane. [b] Cyclohexene was trapped as 1,2-dibromocyclohexane. [c] About 3% of 1-bromo-2-hydroxycyclohexane was detected. Water contamination in the solvent and/or electrolyte is responsible for its formation. [d] Trace amounts of the product mentioned in footnote *c* were observed.

In order to carry out the electro-oxidations at optimized conditions we arbitrarily chose (II) as a model compound and studied its oxidation under various conditions. The change of total product yield in each case was examined. Tables 1—4 summarize the effect of temperature, concentration, supporting electrolyte, and electricity consumption, respectively, on the oxidation of (II). Examination of the results shown in these Tables leads us to the conclusion that employing tetraethylammonium fluoborate as an electrolyte, oxidizing the substrate in 0.5M-concentration at 0 °C, and passing 0.8 F/mol gives the best results under the

TABLE 2

The effect of concentration on the yield of products derived from the electro-oxidation of (II) at 2.5 V at 0 °C

[(II)]/M [a]	mF consumed	% (IIa) [b]	% (IIb) [b]
2.0	4.2	4	1—2
1.0	4.0	17	4
0.5	4.2	60	14
0.2	4.0	20	18
0.05 [c]	4.9	1—2	Trace

[a] In all experiments the background current was 10—25 mA. The initial current was 80—120 mA. All reactions were terminated after passing 4 mF. [b] See footnote *b* for Table 1. [c] Initial current was 50 mA. When [(II)] = 0.025M the initial current was only slightly above the background current.

TABLE 3

The effect of supporting electrolyte on the oxidation of (II) at 2.5 V at 0 °C [a]

Electrolyte (0.2M)	% (IIa)	% (IIb)
LiClO$_4$	33	3
TEAF	60	14
TEAP	45	9
NH$_4$BF$_4$	26	11

[a] [II] = 0.5M. The electrolysis was terminated after passage of 0.8 F/mol. See also footnote *b* for Table 1.

TABLE 4

The effect of *n*-value [a] on the anodic oxidation of (II) at 2.5 V at 0 °C {[(II)] = 0.5M, TEAF electrolyte}

mF [b]	% (IIa)	% (IIb)
1.8	14	3
4.2	60	14
5.7	32	7
8.0	6	6

[a] Number of electrons per molecule. [b] Amount of charge passed per 5 mmol of (II).

conditions studied. Following this conclusion all other substrates, (I) and (III)—(V), were electrolysed under these same conditions. The comparative results are described in Table 5. The formation of olefins was established by adding bromine to the reaction mixture, immediately after the termination of the electrolysis, to form the corresponding dibromocycloalkanes. This was done in order to avoid the possible loss of volatile olefins during work-up.

TABLE 5

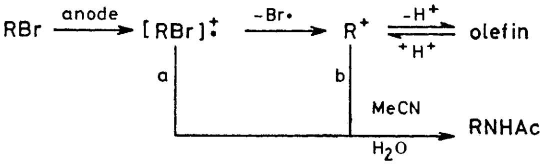
Yield of electro-oxidation products from (I)—(V) [a]

Substrate	% Amide	% 1,2-Dibromo-cycloalkane	% 1-Bromo-2-hydroxy-cycloalkane
(I)	(Ia) 26	(Ib) 1—2	
(II)	(IIa) 60	(IIb) 14	Trace
(III)	(IIIa) 45	(IIIb) 4	Trace
(IV)	(IVa) 60		
(V)	(Va) 45		

[a] [substrate] = 0.5M. TEAF (0.2M) was used as an electrolyte. All electrolyses were carried out at 2.5 V at 0 °C. In certain experiments, small negligible amounts of acetamide were detected. Yields of products (Ia)—(IIIa) are based on the calibration curve made for (IIa). Yields of (Ib)—(IIIb) are based on the calibration curve made for (IIb). Yields of (IVa) and (Va) are based on isolated products.

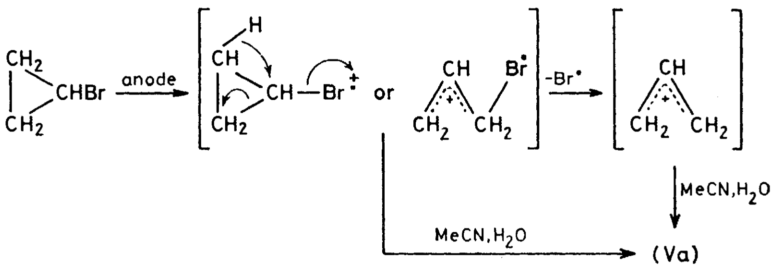
DISCUSSION

The formation of *N*-cycloalkylacetamides and olefins could be rationalized as illustrated in Scheme 1. Alkylated acetamides could be formed either by the attack of the nucleophilic solvent acetonitrile on the cation radical (path a) and/or the attack on a carbenium ion type intermediate (path b). Both mechanisms are feasible and have been discussed previously in detail.[2] Olefin formation could be attributed to proton loss from a carbenium ion. However, due to a high proton concentration in the vicinity of the electrode, certain amounts of the olefins could undergo protonation to regenerate carbenium ions which can then yield acetamides. Therefore, the actual yield of olefins shown in Table 5 may be higher.



SCHEME 1

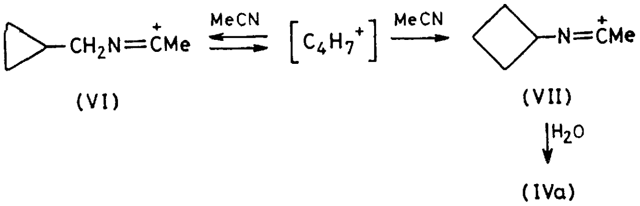
Since five-, six- and seven-membered rings are largely unstrained and have about the same heat of combustion, ring-opening is not expected to accompany their oxidation and, in fact, none of the products isolated from (I)—(III) was derived from cleavage of carbon–carbon σ-bond. In contrast, ring-strain[4] in the three-membered ring gave rise to ring-opening. It is known that although cyclopropyl substrates are extremely resistant to nucleophilic attack,[5] when such attack does occur, the result is generally ring opening rather than substitution.[5,6] Further, it is well established that a positive charge generated on a three-membered ring gives ' contraction ' to an allylic cation,[6,7] and that the ring opening of cyclopropyl cations is an electrocyclic reaction governed by the orbital symmetry rules.[8] Therefore, the formation of allylacetamide (Va) from (V) is not surprising and could be postulated to occur according to Scheme 2. A carbon–bromine bond cleavage could take place after the formation of the cation radical or during the attack of the nucleophilic solvent on the cation radical. Each of these mechanisms is accompanied by skeletal rearrangement in the cyclopropyl ring to form a stable allylic cation. According to the literature,[6,9] there is much evidence that the ring-opening is concerted with the departure of the leaving group. This means that the σ bond provides anchimeric assistance to the removal of the leaving group (an S_N2 type process).



SCHEME 2

Formation of cyclopropene cannot be excluded. However, it was impossible to trap it under our experimental conditions. According to literature reports it is stable only as a solid at liquid-nitrogen temperatures and on warming even to −80 °C it rapidly polymerizes.[10]

Although four-membered rings also exhibit ring strain,[11] since it is less than for cyclopropanes they are less easily opened. Until now there is no evidence which requires that the secondary cyclobutyl cation be intermediate in solvolytic reactions. It is also known that the cyclopropylmethyl cation is kinetically more stable [12] since both σ-bonds of the cyclopropyl ring help to stabilize the positive charge due to their π-bond character. However, in spite of the latter argument, the oxidation of (IV) yielded only one type of amide, (IVa), with a cyclobutyl ring. This result may indicate that (IVa) could be formed either *via* S_N2-type displacement (path a in Scheme 1), or through the following mechanism which was suggested by Laurent and his co-workers[13] for the anodic oxidation of iodomethylcyclopropane and iodocyclobutane:



They assume that both acetonitrilium ions, (VI) and (VII), are formed from each of the iodo-compounds mentioned above. The cyclopropylcarbinyl intermediate (VI) isomerizes to the thermodynamically more stable one,[14] namely the corresponding cyclobutyl isomer (VII) when the electrolysis duration was sufficiently long.[13] In fact, in the present work we have used a much higher concentration of (IV) and, consequently, a longer reaction time. Therefore, our result is in full agreement with Laurent's observations.

In an effort to detect cyclobutene from (IV) nitrogen was continuously passed through the anolyte during the electrolysis of (IV). The gaseous stream which might have entrained cyclobutene was passed from the cell through a solution of bromine in tetrachloromethane. No dibromo-product was identified after removal of the excess of bromine with aqueous thiosulphate and the tetrachloromethane by evaporation.

The fate of the bromine fragment is not clear at present. Free Br_2 was not observed although its formation cannot be excluded. Small amounts of, for example, 1,2-dibromocyclohexane which were obtained before addition of bromine to the electrolysis mixture, could be formed from a direct addition of Br_2 (formed by recombination of bromine radicals) to olefin (IIb) and/or by addition of other positively charged bromine species (*vide infra*). However, not all the bromine undergoes recombination; some of the bromine species would have diffused away to the cathode compartment to be reduced to Br^-. This was confirmed qualitatively by the Ag^+ test followed by addition of ammonia solution. Assuming the probability for the oxidation of bromine radicals is higher in comparison with their recombination to give bromine molecules, one would expect that a reaction, such as the following, would take place:

$$Br\cdot + MeCN \xrightarrow{\text{anode}} Me\overset{+}{C}{=}NBr$$

The $Me\overset{+}{C}{=}NBr$ intermediate could explain the formation of acetamide in acidic media, which was detected in small amounts in some of the product mixtures. Bromine(I) could also be present in solution in other forms and the investigation on such species is in progress in our laboratory.

Different possibilities arise if bromine radicals will not undergo further oxidation but may abstract a hydrogen from some other sources, *e.g.* the solvent, or supporting electrolyte. Indeed, $BrCH_2CN$ from the solvent and $Et_2NC_2H_4Br$ from the electrolyte were formed and detected by means of mass spectrometry.

EXPERIMENTAL

Materials.—Acetonitrile (Fluka 99.5%) was purified by distillation from phosphorus pentaoxide under nitrogen and stored over 4 Å molecular sieves. Anhydrous lithium perchlorate (Alfa Products) was used without any further treatment. Tetra-alkylammonium fluoborates and perchlorates were purchased from Fluka AG and used without further purification. All cyclic bromoalkanes were commercial samples (Aldrich and Fluka AG).

Instrumentation.—A Perkin-Elmer IR spectrometer model 137 and Varian XL 100 NMR spectrometer were used for structure determination. Mass spectra were measured with a Varian model MAT 112 CI GC/MS system. G.l.c. analyses were performed with a Varian Aerograph model 920 gas chromatograph equipped with a thermal conductivity detector. The potentiostat employed was a Princeton Applied Research model 173. Coulometry during preparative electrolysis was performed with a counter constructed from an Acromag integrator-totalizer. A Universal Programmer model 175 from Princeton Applied Research was used as a function generator to pulse the anode potential during preparative oxidations and to determine scan rates during cyclic voltammetry measurements. The recorder employed during these cyclic experiments was a model 26000 A4 X-Y recorder from Bryans.

Cyclic Voltammetry.—Voltammograms were recorded for each cyclic bromoalkane in a two-compartment cell containing twice-distilled acetonitrile and tetrabutylammonium fluoborate as supporting electrolyte. The Ag/0.1M-$AgNO_3$ reference electrode was separated from the working electrode by a fine glass frit *ca.* 5 mm in diameter. The auxiliary electrode was a cylindrical platinum gauze and the working electrode a platinum wire sealed in glass and ground smooth making a small platinum button. The voltammograms showed no cathodic peak corresponding to reduction of an initially formed cation radical. Voltammograms were recorded from 0 to 3 V and all alicyclic bromides listed in Table 5 show an ill-defined oxidation peak in the range 2.5—2.7 V except for cyclopropyl bromide which gave a well-defined wave at 2.4 V.

Authentic Samples.—*N*-Alkylacetamido-derivatives were prepared by two procedures described elsewhere.[2] The availability of the starting material determined the method of choice. Thus, aminoalkanes were treated with acetic anhydride and tertiary alcohols were treated with H_2SO_4 in acetonitrile. 1,2-Dibromocycloalkanes were prepared by treating the corresponding olefin with Br_2 in CCl_4. The n.m.r. data for all products listed in Table 5 were consistent with those of the comparison samples. The amides show characteristic absorptions in the i.r. regions 1 650, 1 670, and 3 300 cm^{-1}. Their mass spectra gave typical cleavages due to loss of C_2H_3O, C_2H_4NO, and C_2H_5NO from the molecular ion. Amide (IVa) showed a strong mass peak at 98 due to a loss of Me. All mass spectra of the dibromo-compounds gave typical ' triplets ' each at the region of its molecular ion. Loss of Br and HBr fragments were also typical.

Preparative Oxidations.—For all preparative anodic reactions listed in this work, a modified ' H ' cell was employed as a three-compartment electrochemical cell. The anode compartment held *ca.* 50 ml of anolyte, the cathode held 30 ml of catholyte, and the reference held 2 ml of 0.1M-$AgNO_3$, in acetonitrile. The anode compartment was separated from the cathode by a 3-cm diameter medium glass frit and the reference by a 1-cm diameter fine glass frit at one end. The anode compartment was also fitted with a ground-glass lid. The lid had an inlet and outlet for the passage of nitrogen gas. A cylindrical platinum gauze of 2.5 cm in diameter was employed as the anode and was suspended from the lid. A stainless-steel sheet was used as the cathode, and a silver wire for the reference. The anolyte was stirred with a magnetic stirrer and the electrochemical cell was immersed in a cold bath, if required. In some preparative oxidations, the anode potential was pulsed to *ca.* 0 for 1 s each 25 s. This was generally unnecessary, however, and had no discernible effect on the product. The potential was set at 2.5 V and the reactions were arbitrarily terminated, usually after passage of *ca.* 0.8 F/mol of added substrate. The work-up procedure consisted of an addition of bromine to the anolyte until it became yellow-brownish and then treated with an aqueous solution of sodium bisulphite to destroy the excess of bromine. (Bromine was not added in certain experiments in which brominated products resulted from the electrolysis were to be detected.) This was followed by evaporation of much of the acetonitrile (caution: not to dryness. If perchlorate electrolyte is used the anolyte contains perchloric acid!), addition of water, and extraction twice with chloroform and twice with methylene chloride. The combined organic layers were washed once with water and then dried ($MgSO_4$). After filtration and evaporation to an oil the product mixtures were isolated by preparative g.l.c. using a 10% SE-30 column, 2 m × $\frac{1}{4}$ in, on Chromosorb W. The products isolated were characterized by n.m.r. and g.l.c. comparisons with authentic samples.

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REFERENCES

[1] J. Y. Becker and M. Münster, *Tetrahedron Letters*, 1977, 455.

[2] J. Y. Becker, *J. Org. Chem.*, 1977, **42**, 3997.

[3] F. Vincent, R. Tardivel, and P. Mison, *Tetrahedron Letters*, 1975, 603; *Tetrahedron*, 1976, **32**, 1681.

[4] E. Vogel, *Angew. Chem.*, 1960, **72**, 4.

[5] J. D. Roberts and V. C. Chambers, *J. Amer. Chem. Soc.*, 1951, **73**, 5034.

[6] C. H. DePuy, L. G. Schnack, and J. W. Hausser, *J. Amer. Chem. Soc.*, 1966, **88**, 3343.

[7] P. S. Skell and S. R. Sandler, *J. Amer. Chem. Soc.*, 1958, **80**, 2024; H. M. Frey, *Adv. Phys. Org. Chem.*, 1966, **4**, 147.

[8] C. H. DePuy, *Accounts Chem. Res.*, 1968, **1**, 33; U. Schöllkopf, *Angew. Chem. Internat. Edn.*, 1968, **7**, 588.

[9] C. W. Jefford and R. T. Medary, *Tetrahedron*, 1967, **23**, 4123; C. W. Jefford and W. Wojnarowski, *ibid.*, 1969, **25**, 2089; P. v. R. Schleyer, G. W. Van Dine, U. Schöllkopf, and J. Paust, *J. Amer. Chem. Soc.*, 1966, **88**, 2868; J. W. Hausser and J. T. Uchic, *J. Org. Chem.*. 1972, **37** 4087

[10] M. J. Schlatter, *J. Amer. Chem. Soc.*, 1941, **63**, 1733; K. B. Wiberg and W. J. Bartley, *ibid.*, 1960, **82**, 6375; W. M. Stigliani, V. W. Laurie and J. C. Li, *J. Chem. Phys.*, 1975, **62**, 1890.

[11] A. Wilson and D. Goldhamer, *J. Chem. Educ.*, 1963, **40**, 504.

[12] K. B. Wiberg and A. J. Ashe, III, *J. Amer. Chem. Soc.*, 1968, **90**, 63.

[13] E. Laurent and R. Tardivel, *Tetrahedron Letters*, 1976, 2779.

[14] M. Hanack and M. J. Schneider, *Angew. Chem. Internat. Edn.*, 1967, **6**, 666.