RITTER REACTIONS. II. REDUCTIVE DEAMIDATION OF N-BRIDGEHEAD AMIDES.

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<u>Abstract</u>: Adamantyl- or homoadamantyl-derived N-bridgehead amides are converted in high yields into hydrocarbon derivatives on prolonged reflux in ethanol and 50% sulphuric acid (1:1 by volume). This process probably involves  $A_{\rm AL}$  hydrolysis to the tertiary carbonium ion, followed by hydride abstraction from the ethanol solvent.

7,11-Dimethylene-6,7,8,9-tetrahydro-5,9-propano-5*H*-benzocycloheptene (1) undergoes an efficient intramolecular cyclisation and Ritter reaction in the presence of strong acid and acetonitrile to yield the acetamide derivative (2)<sup>1</sup>. When this amide was refluxed in a mixture of ethanol and 50% sulphuric acid (1:1 by volume) a less polar compound was formed slowly, the reaction being essentially complete after 46 hours. Purification of this material on alumina gave a 60% yield of a hydrocarbon product whose data<sup>2</sup> indicated the structure 7-methyl-6,7,8,9,10,11-hexahydro-5,9:7,11-dimethano-5*H*-benzocyclononene (3).



Confirmation of this structural assignment was made by reduction of the known chloro derivative (4)<sup>3</sup> using tributyltin hydride and azobis(isobutyronitrile) (AIBN) in refluxing toluene following the method of Greene and Lowry<sup>4</sup>. The alkane obtained had identical i.r.,  ${}^{\rm L}$ H n.m.r. and  ${}^{\rm L3}$ C n.m.r. spectra to the previous sample of (3).

This novel reductive deamidation reaction of the N-bridgehead amide group appears to be general for adamantyl- and homoadamantyl-based systems. Reaction of 1-acetamidoadamantane (5)<sup>5</sup> under the same conditions afforded a 97% yield of adamantane (6), identical to an authentic sample by m.p. and by mass, i.r.,  ${}^{1}_{H}$  n.m.r. and  ${}^{13}$ C n.m.r. spectroscopy. Similar reaction of 1-acetamido-2,2,5,6,6-pentamethyladamantane (7)<sup>6</sup>, but refluxing for 4 days, produced an 84% yield of 1,2,2,6,6-pentamethyladamantane (8)<sup>7</sup>.





The simplest and most reasonable explanation of this amide to hydrocarbon reduction is a one-flask combination of two previously-known processes, namely generation of a tertiary carbonium ion at the bridgehead site, followed by hydride transfer from the ethanol solvent.

Although amide hydrolysis under acidic conditions normally proceeds by N-acyl cleavage to yield the amine, a number of pathways may be envisioned involving N-alkyl fission, for example that proposed by Haaf<sup>8</sup> (which is essentially the reverse of the Ritter reaction):

$$R_3C-NH-C-R \xrightarrow{H_2SO_4} R_3C-N \equiv C-R \xrightarrow{+} R_3C + N \equiv C-R$$

or the  $A_{\rm AL}$  process of Lacey<sup>9</sup>:

$$R_3^{C-NH-C-R}$$
  $\xrightarrow{H_3^{O}}$   $R_3^{C-NH_2^{-C-R}}$   $\xrightarrow{+}$   $R_3^{C}$   $+$   $NH_2^{-C-R}$ 

In his studies on the latter process Lacey carried out conversions such as the following, using 30% sulphuric acid under reflux conditions.

Such products are clearly carbonium ion derived, while the acidity of the reaction conditions is comparable to ours. More recently, Adolph has used the N-t-butyl function as a protecting group in the synthesis of certain fluoronitroamides<sup>10</sup>, while Stepanov<sup>11</sup> found that reflux of 1- or 3-acetamidohomoadamantane in concentrated hydrochloric acid resulted in deamidation and formation of chlorinated products.

There is therefore reasonable precedent for N-alkyl cleavage of amides under acidic conditions where a favourable<sup>12</sup> tertiary carbonium ion can result. It is well established through the work of Schleyer, Olah, and other workers<sup>13</sup> that such tertiary carbonium ions can abstract hydride from suitable organic donor molecules (even under extreme acid conditions) to produce hydrocarbons. The following sequence of events is therefore suggested as the most likely explanation of our observations.



## TYPICAL EXPERIMENTAL PROCEDURE:

50% Aqueous sulphuric acid (30 ml) was added to a solution of amide (7) (0.61 g, 2.33 mmol) in ethanol (30 ml) and the mixture heated at reflux. Aliquots were withdrawn at intervals and analysed by t.l.c. to monitor the progress of the deamidation reaction. After 4 days the mixture was cooled, extracted thoroughly with ether, then the combined extracts washed ( $H_2O$ ), and dried ( $Na_2SO_4$ ). Solvent was distilled off from the filtrate to give an oil which was purified by elution through a short column of alumina using pentane, and then distilled to give the pure hydrocarbon (8) (0.40 g, 84%).

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- 1 Ritter Reactions. I. Amini, R. Bishop, and G. Burgess, Aust. J. Chem., (in press).
- 2 <u>Data for (3)</u>:
  - M.p.  $46-48^{\circ}$ C.  $M/z^{+}$  213(23%), 212(M<sup>+</sup>, base peak), 198(11), 197(62), 183(5), 169(6), 156(11), 155(49), 143(19), 142(16), 141(51), 130(7), 129(43), 128(24), 127(5), 117(9), 115(22), 93(5), 91(15), 85(6), 81(8), 77(6), 71(14), 69(15), 67(6), 58(24), 56(16), 43(19) and 41(21). (Found: C,90.30; H,9.66.  $C_{16}H_{20}$  requires C,90.51; H,9.49%).  $v_{max}$ (liquid film) 3080w, 3040m, 2970s, 2925s, 2860s, 1500m, 1460s, 1445s, 1385m, 1365m, 1310w, 1270w, 1225m, 1190m, 1110w, 1095w, 1080w, 1050m, 1005w, 950m, 940m, 760s, 620m cm<sup>-1</sup>.  $^{1}_{H} \delta$  (CDCl<sub>3</sub>) 0.85, s, 3H; 1.5-1.9, m, 10H; 2.1-2.3, m, 1H; 2.8-3.0, m, 2H; 7.04, s, 4H.  $^{13}C \delta$  ( $C_{6}D_{6}$ ) 30.1,s; 30.5,d; 33.4,q; 35.0,t; 41.9,d; 42.2,t; 43.5,t; 126.4,d; 128.4, d; 147.6,s. [The observation of ten carbon signals indicates that the mirror plane symmetry of the starting material (2) is retained in the product, and rules out the involvement of a rearrangement process].
- 3 Amini, and R. Bishop, Aust. J. Chem., (1983), 36, 2465.
- 4 F.D. Greene, and N.N. Lowry, J. Org. Chem., (1969), 32, 882.
- 5 H. Stetter, J. Mayer, M. Schwartz, and K. Wulff, Chem. Ber., (1960), 93, 226.
- 6 Amini, M.Sc. thesis (U.N.S.W.), (1982).

## 7 <u>Data for (8)</u>:

B.p.  $218-230^{\circ}$ C. (Found: C,87.23; H,12.59. C<sub>15</sub>H<sub>26</sub> requires C,87.30; H,12.70%).  $v_{max}$  (liquid film) 3000s, 2940s, 2890s, 1465s, 1395s, 1370m, 1350w, 1175m, 1155m, 1105w, 1060m, 1000m, 985w, 890m, 755w cm<sup>-1</sup>. <sup>1</sup>H  $\delta$  (CDCl<sub>3</sub>) 0.69, s, 3H, 1-methyl; 0.96, s, 6H, 2,2-dimethyl; 0.99, s, 3H; 1.03, s, 3H; 1.1-1.9, m, 11H. <sup>13</sup>C  $\delta$  (CDCl<sub>3</sub>) 23.5,q; 23.9,q; 26.9,q; 27.1,q; 28.3,t; 34.1,s; 34.7,s; 35.9,t; 37.9,s; 38.7,d; 39.8,d. [Compound (8) has mirror plane symmetry (through carbons 1,2,3 and 6) which is not present in the starting material (7). It therefore exhibits eleven carbon signals, with the C2 methyl groups being equivalent , but the C6 methyl groups being non-equivalent. This is also shown by the methyl group signals in the proton n.m.r. spectrum].

- 8 W. Haaf, Chem. Ber., (1963), 96, 3359.
- 9 R.N. Lacey, J. Chem. Soc., (1960), 1633.
- 10 H.G. Adolph, J. Org. Chem., (1972), 37, 747.
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- 12 In applying this procedure to new systems consideration should be taken of the ease of formation of the potential carbonium ion, and the possibility of rearrangement to give an ion of lower energy.

13 For example :

W.D. Graham, and P.v.R. Schleyer, <u>Tetrahedron Lett.</u>, (1972), 1179; J.S. Wishnok,
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