

FREE-RADICAL HALOGENATION OF 1-AZA-ADAMANTANE<sup>1</sup>,

by

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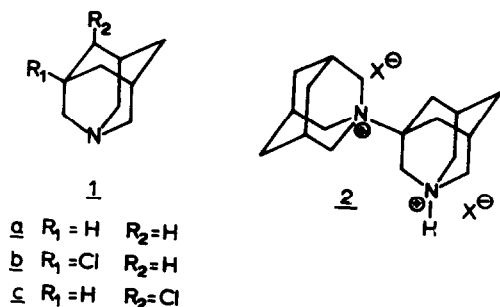
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Although radical reactions of tertiary amines have been postulated to play an essential role in certain biological processes<sup>2</sup> only scarce chemical information is available<sup>3</sup> on this type of reaction. Aiming at novel routes to 3-halogenated 1-aza-adamantanes we have investigated the reaction of 1a with different halogenating agents.

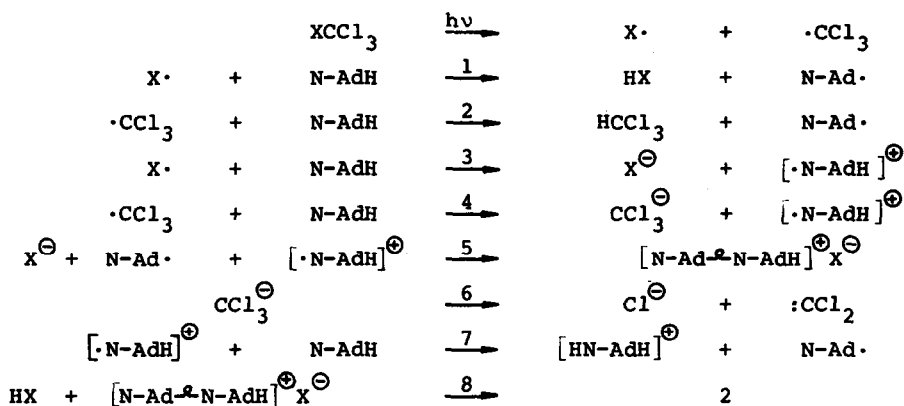
Irradiation<sup>4</sup> of 1a in presence of BrCCl<sub>3</sub> immediately resulted in the formation of a white precipitate; the same product 2 was obtained on reaction of 1 with BrCCl<sub>3</sub> in presence of Bz<sub>2</sub>O<sub>2</sub>. As micro analysis of 2 revealed the presence of both Cl<sup>⊖</sup> and Br<sup>⊖</sup> the reaction was repeated with CCl<sub>4</sub> as halogen source.



Again a crystalline compound was formed in a yield of 81% based upon converted 1a, which on the basis of its analytical data was formulated as the dimer 2, (x = Cl) mp >300°C (dec)<sup>5</sup>. The latter product was also formed upon photochlorination of 1a with CCl<sub>3</sub>SO<sub>2</sub>Cl (yield 64%). In none of the experiments

the formation of 1b and 1c could be detected although GLC-analysis of the supernatant indicated the presence of  $\text{CHCl}_3$ . The possibility of 2 arising from a combination of firstly formed 1b with 1a was ruled out by irradiation in benzene (quartz vessel) of a mixture of 1a and 1b which gave back only the starting materials almost quantitatively.

In agreement with recently found results<sup>6</sup> on the behaviour of polyhaloalkanes in electron-transfer reactions, the following sequence of main processes is conceivable : (  $\text{N-AdH} \equiv \underline{1a}$  ,  $[\text{N-Ad-}^{\ominus}\text{N-AdH}] \text{X}^{\ominus} \equiv \underline{2}$  )



In view of the number of possible routes<sup>7</sup> no clear mechanistic results have been obtained as yet, although most likely reactions 1 - 8 have to be involved. Two general aspects, however, may be emphasized :

- (i) the high efficiency of the combination of the  $\text{N-Ad}\cdot$  and  $[\cdot\text{N-AdH}]^{\oplus}$  species<sup>8</sup> and (ii) the easy mode of reaction of tertiary amines with polyhalomethanes<sup>9</sup>.

From the foregoing results it became obvious that halogen sources of different type had to be used to achieve our synthetic goal. While N-halo-succinimides<sup>10</sup> and sulfonyl chloride gave no positive results the use of  $\text{tBtOCl}$  afforded the chloro-derivatives 1b and 1c in yields indicated in the table.

TABLE

tBtOCl <sup>a</sup>	time in hr	T(°C)	<sup>b</sup> W	<sup>c</sup> <u>la</u>	<sup>c</sup> <u>lb</u>	<sup>c</sup> <u>lc</u>	<sup>d</sup> <u>lb</u> (%)
1.0	1	r.t.	0,100	4	4	1	37
1.0	2	r.t.	0,1165	3	4	1.5	45
1.0	20	r.t.	0,1105	4.5	7	2	46
1.5	2	r.t.	0,1290	1	4	1	59
2.0	4	r.t.	0,100 <sup>e</sup>				-
1.0	6	-10°	0,1125	1.5	4.5	1	51

- a) mmol of tBtOCl  
 b) weight of solid material obtained after work-up and sublimation in g  
 c) determined by PMR-analysis of the solid material  
 d) calculated on the amount of la consumed  
 e) in this experiment significant quantities of dichlorinated material were obtained which prevented accurate analysis.

In a typical experiment 1.0 mmol of la together with the amount of tBtOCl in 10 ml of benzene was irradiated in a pyrex vessel for the time indicated. After removal of small quantities of solid material (la-HCl) the filtrate was evaporated and the remaining solid purified by sublimation. The 3-Cl derivative was obtained as its HOTs-salt, mp lb-HOTs, 147-148°C, PMR  $\delta$ (CDCl<sub>3</sub>) 3.61 s (2H) NCH<sub>2</sub>-CCl, 3.52 s (4H) NCH<sub>2</sub>. The data for lb, mp 130°C (sublimation at 70°C) PMR  $\delta$ (C<sub>6</sub>D<sub>6</sub>) 3.20 s (2H) NCH<sub>2</sub>-CCl, 2.69 s (4H) NCH<sub>2</sub>.

These results illustrate the striking difference in photochemical behaviour of la towards reagents capable of electron-transfer and other halogenating agents. The ratio lb : la given in the table indicates a similar selectivity pattern as has been found in the bromination of la<sup>11</sup>.

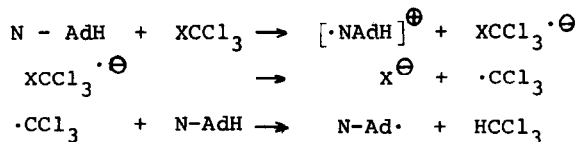
Results of different types of radical reactions will be published separately.

LITERATURE AND REFERENCES

1. Aza-Adamantane Part VIII.

For Part VII : ref. 11.

2. W.A. Pryor, "Free Radical Pathology" in Chem.Eng.Nws, June 7 (1971) p.51.
- 3a. S. Matsuda, H. Kokado and E. Inoue, Bull.Chem.Soc.Japan, 43, 2994 (1970).
- b. S.D. Ross, Tetrahedron Letters, 1237 (1973).
4. Irradiation was carried out neat or in benzene solution in quartz or pyrex vessels depending on the nature of the halogen compound (f.i. BrCCl<sub>3</sub>, CCl<sub>3</sub>SO<sub>2</sub>Cl pyrex ; CCl<sub>4</sub> quartz). A Philips SP-500 (high-pressure) mercury lamp was used as a light source.
5. For all new compounds satisfactory analytical data have been obtained.
6. S. Limatibul and J.W. Watson, J.Org.Chem., 37, 4491 (1972).
7. Alternative routes are <sup>7a</sup> :



The formation of Cl<sup>⊖</sup> in the reaction of BrCCl<sub>3</sub>, however, necessitates the involvement of the CCl<sub>3</sub><sup>⊖</sup> anion.

- 7a. For the dissociation of XCCl<sub>3</sub><sup>⊖</sup> see :
- N.R. Daly and R.G. Ridley, Nature, 202, 895 (1964).
8. Other methods for generating the NAd· radical are currently investigated.
9. Tertiary amines react spontaneously with XCCl<sub>3</sub> at ambient temperature either upon UV-irradiation or after addition of radical initiators. Depending on the type of amine used more or less stable precipitates are formed. Examples of amines used are NEt<sub>3</sub>, N-Me-pyrrolidine, N-Me-morpholine. In the reaction of NEt<sub>3</sub> the formation of CHCl<sub>3</sub> was demonstrated while hydrolysis of the precipitate afforded NEt<sub>3</sub> back together with CH<sub>3</sub>C<sup>H</sup>=O. Further investigation is in progress.
10. I. Tabushi, J. Hamuro and R. Oda, J.Am.Chem.Soc., 89, 7128 (1967).
11. W.N. Speckamp, J. Dijkink and A.W.J.D. Dekkers, Tetrahedron Letters, accompanying communication.