passing the decomposition solution through a small column of Florisil (2 mm × 4 cm in a small filter stem) to remove the colored material. Isolated yields were approximately 85–90% working on a scale of 40–150 mg of **4a**. Recrystallization of the solid formed gave white crystals, mp 83–85°.

Trapping Experiments. A.—The decomposition procedure described above was repeated, except that when the tube was opened, water was added and the mixture shaken well. Several extractions with water were performed and the aqueous extracts placed togenter in a flask containing freshly prepared 2,4-dinitrophenylhydrazine solution.[19] An immediate precipitate formed which was redissolved by heating the solution on a steam bath. The solution was allowed to cool and filtered to give the 2,4-dinitrophenylhydrazone, mp 156–157° (lit.[5] 160°).

B.—The decomposition tube was attached to a stopcock. After 1.5 hr, the stopcock was opened and a 1-ml sample (0.9 *M*) of 2-methyl-2-nitrosopropane in benzene was added. The tube cooled, and a sample was placed in an esr tube. The spectrum consisted of a triplet, $J \approx 15.5$ G.

2-Methyl-2-nitrosopropane was synthesized using literature methods illustrated in the reaction scheme below.

$$(CH_3)_3CNH_2 \xrightarrow{KMnO_4} (CH_3)_3CNO_2{}^{20}$$

$$(CH_3)_3CNO_2 \xrightarrow[Zn]{NH_4Cl} (CH_3)_3CNHOH{}^{21}$$

$$(CH_3)_3CNHOH \xrightarrow[OH^-]{Br_2} (CH_3)_3CNO{}^{22}$$

(19) Reference 7, p 111.
(20) N. Kornblum, *Org. React.*, **12**, 133 (1962).
(21) F. D. Greene and J. F. Pazos, *J. Org. Chem.*, **34**, 2269 (1969).
(22) W. D. Emmons, *J. Amer. Chem. Soc.*, **79**, 6522 (1957).

Control Experiments.—The same decomposition conditions were applied to **3c**, **4c**, and **10**. Analysis by nmr of the crude reaction mixture showed no decomposition.

In another experiment, 100 mg of **4a** was dissolved in benzene, and the solution was extracted five times with 1 ml of D_2O. The benzene layer was dried over $MgSO_4$ and the solvent removed. The product was recrystallized from CH_3OD. Mass spectral analysis showed it to contain 60% deuterium atom/molecular. A 52-mg sample of this *N*-deuterio-**4a** was dissolved in 1 ml of benzene and decomposed as described above. The nmr spectrum of the decomposition product was identical with that obtained from normal **4a** (see Figure 1).

Registry No.—**1**, 30765-45-8; **2**, 30765-46-9; **3a** HBr, 30765-47-0; **3b** HCl, 30765-48-1; **3c**, 30765-49-2; **4a**, 30765-50-5; **4b**, 30765-51-6; **4c** HCl, 30765-52-7; **4c** picrate, 30765-53-8; **5**, 30765-54-9; **6**, 30765-55-0; **7**, 30765-56-1; **8**, 30768-30-0; **8-*d***, 30768-31-1; **10**, 30768-32-2.

Acknowledgments.—We wish to thank Mr. Alan Marion for the electron spin resonance spectra and Mr. Dwayne Campbell for the mass spectral work. Both are of the Department of Chemistry, University of Nebraska. The authors also wish to thank Dr. Alfred Hassner, Department of Chemistry, University of Colorado, for helpful discussions concerning this work. This work was supported in part by a Special Departmental Science Development Award to the Department of Chemistry from the National Science Foundation No. GU-2054. One of us (G. G.) held an Avery Fellowship from the University of Nebraska and wishes to acknowledge this award.

Carbon–Sulfur Cleavage of 1-Adamantyl Sulfides[1]

K. K. KHULLAR AND LUDWIG BAUER*

Department of Chemistry, College of Pharmacy, University of Illinois at the Medical Center, Chicago, Illinois 60680

Received February 8, 1971

Acid-catalyzed carbon–sulfur cleavage at the bridgehead of some 1-adamantyl sulfides was encountered. β-(1-Adamantanethio)ethylamine and ε-(1-adamantanethio)pentylamine were converted by boiling hydrochloric acid to 1-chloroadamantane (80–90%) and the corresponding ω-mercaptoalkylamine. A similar cleavage was exhibited by *S*-(1-adamantyl)isothiuronium bromide and several amidine derivatives of β-(1-adamantanethio)-ethylamine. By direct contrast, 1-methyl- and 1-ethylthioadamantane were recovered quantitatively under these conditions. 1-Adamantyl alkyl ethers were converted by hydrochloric acid at 25° to 1-chloroadamantane, irrespective of the nature of the substituent in the alkyl side chain. Whereas 1-adamantanol was transformed to 1-chloroadamantane (92%) by cold concentrated hydrochloric acid, 1-adamantanethiol remained unchanged even on boiling with this acid.

During an attempted acid-catalyzed hydrolysis of the thiosulfate group in the α-amidinium Bunte salt **20** to the corresponding thiol by means of hot concentrated hydrochloric acid, cleavage of the sulfide moiety took place and 1-chloroadamantane (**1**) was isolated in 75% yield. This unexpected displacement at the 1-adamantane bridgehead prompted us to investigate this type of reaction further. In view of the facile solvolysis of 1-adamantyl ethers and sulfonates,[2-4] it was of further interest to compare the relative stability of similarly constituted 1-adamantyl ethers and sulfides and related systems toward hydrochloric acid.

The behavior of 1-adamantanol (**2**) and the corresponding thiol **12** toward hot concentrated hydrochloric acid was investigated first. Reaction of **2** furnished 1-chloroadamantane (**1**, 94%) after 0.5 hr, while **12** was recovered quantitatively even after 3 hr. This conversion of **2** to **1** appeared to be a simpler procedure than the one reported previously using thionyl chloride.[4]

Some simple ethers and thioethers in this series were examined next. It had been found that on shaking with cold concentrated hydrochloric acid for a short time, 1-methoxyadamantane (**3**) yielded **1** (96.5%),[3] but it was claimed that a similar cleavage of the ethyl analog **4** was more difficult.[3] We have found that **4**[2] was converted quantitatively to **1** by cold concentrated

(1) Support for this work by the U. S. Army Medical Research and Development Command (Contract DADA 17-69-C-9110) is gratefully acknowledged.
(2) D. N. Kevill, K. C. Kolwyck, and F. L. Weitl, *J. Amer. Chem. Soc.*, **92**, 7300 (1970).
(3) F. N. Stepanov, V. F. Baklan, and S. S. Guts, *Chem. Abstr.*, **65**, 627 (1966) [*Sint. Prir. Soedin., Ikh Analogov Fragmentov*, 95 (1965)].
(4) H. Stetter, M. Schwarz, and A. Hirschhorn, *Chem. Ber.*, **92**, 1629 (1959).

hydrochloric acid at 25° in 10 min. In view of this facile ether cleavage, it seems logical that the ethers **5–11** were transformed readily to **1** by hydrochloric acid, irrespective of the nature of the side-chain substituents.

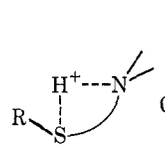
However, the methyl and ethyl thioethers **13** and **14** stubbornly resisted cleavage with boiling hydrochloric acid and were recovered unchanged. The surprising departure from this pattern was witnessed when the alkyl sulfide side chain contained a basic substituent. At 25°, β- (1-adamantanethio)ethylamine (**15**) formed a stable hydrochloride with cold concentrated hydrochloric acid but at reflux (3 hr) decomposed to **1** (90%) and β-mercaptoethylamine. The extent of this cleavage appeared to be related to the acid concentration.

For example, 6 *N* hydrochloric acid at 100° (24 hr) afforded only 34% of **1**, with 50% of **15** being recovered. This cleavage was slowed down even further when boiling 1 *N* hydrochloric acid was utilized (8 hr) when only 11% of 1-adamantanol (**2**) was isolated, together with 50% of **15**. When the amino group in **15** was converted to the benzamide **17**, the ability for C–S scission virtually disappeared. Boiling concentrated hydrochloric acid (3 hr) transformed **17** to **1** in 9% yield, with 90% of starting material being unchanged. No cleavage of the thioether group was observed at all in the sulfonamide **18** derived from **15**. It would appear that an amino function built into the side chain was essential for this substitution to take place. Addition of triethylamine to the reaction mixture containing 1-ethylthioadamantane (**14**) and hot hydrochloric acid did not induce decomposition of this sulfide.

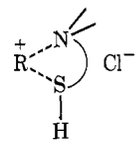
To test if the proximity of the amino group to the sulfide function was essential, ε-(1-adamantanethio)-pentylamine (**16**) was boiled with hydrochloric acid (3 hr). There were isolated **1** (83%) and ε-mercaptopentylamine (as the *N,S*-dibenzoyl derivative). In view of the results presented above, it is not surprising that the two amidine derivatives, based on **15**, *viz.*, **19** and **20**, were split to produce **1** in 92 and 75%, respectively.

One other interesting observation bears on this problem. When 1-bromo- or 1-chloroadamantane was allowed to react with thiourea in boiling acetic acid containing hydrobromic acid, the isothiuronium bromide **21** was isolated quantitatively. However, exposure of **21** to boiling concentrated hydrochloric acid (3 hr) seemingly reversed this displacement to form **1** in 95% yield. The conversion of **21** to **1** was only 34% complete in 0.5 hr, 43% of **21** being recovered. Interestingly enough when concentrated hydrochloric acid was replaced by a mixture of the acid and tetrahydrofuran (1:1), this displacement was prevented, 75% of **21** being recovered. The sensitivity of solvents for displacement at the 1-adamantane bridgehead is well known[5] but this aspect was not pursued further.

The amino group in the side chain appears to play an important role in this cleavage. It could exert a dual role by first assisting in the protonation of the sulfide group to form **24** and then stabilizing an ion pair, involving the 1-adamantyl carbonium ion in close contact with the nucleophilic nitrogen and sulfur atoms **25** (R = 1-adamantyl). Intrusion by chloride ion into **25** is concentration dependent and takes place in the medium employed to form the neutral 1-chloroadamantane.

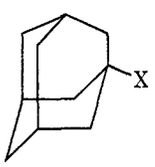


24



25

The related displacement by hydrochloric acid of the amide group in 1-acetamidoadamantane **22**, to form **1** (98%),[4] and the analogous reaction in the 3,5-dimethyl analog to produce 1-chloro-3,5-dimethyladamantane (62%),[6] bears on this problem. It is suggested that the protonated amide can function in similar fashion as outlined for **24** and **25**. The amide function is essential, since 1-aminoadamantane is recovered unchanged on boiling with hydrochloric acid. We have also found that 1-adamantyl isothiocyanate (**23**) was stable to hot concentrated hydrochloric acid.



Compd	X
1	Cl
2	OH
3	OCH_3
4	OC_2H_5
5	$O(CH_2)_2NH_2$
6	$O(CH_2)_3NH_2$
7	$OCH(CH_3)CH_2NH_2$
8	$O(CH_2)_2NHC(=NH_2^+)CH_2Cl\ Cl^-$
9	$O(CH_2)_2NHC(=NH_2^+)CH_2S_2O_3^-$
10	$O(CH_2)_2NHC(=NH_2^+)CH_2S_2O_3^-$
11	$OCH(CH_3)CH_2NHC(=NH_2^+)CH_2S_2O_3^-$
12	SH
13	SCH_3
14	SC_2H_5
15	$S(CH_2)_2NH_2$
16	$S(CH_2)_5NH_2$
17	$S(CH_2)_2NHCOC_6H_5$
18	$S(CH_2)_2NHSO_2C_6H_4CH_3$-*p*
19	$S(CH_2)_2NHC(=NH_2^+)CH_2Cl\ Cl^-$
20	$S(CH_2)_2NHC(=NH_2^+)CH_2S_2O_3^-$
21	$SC(=NH_2^+)NH_2\ Br^-$
22	$NHCOCH_3$
23	N=C=S

Experimental Section[7]

1-Adamantanethiol.—A mixture of 1-bromoadamantane[8] (10.75 g, 0.05 mol), thiourea (7.6 g, 0.1 mol), 48% HBr (25 ml), and acetic acid (50 ml) was heated under reflux for 3 hr. On cooling, **21** crystallized out (quantitatively): mp 231–232° (from ethanol); pmr (CF_3CO_2H) two broad singlets, δ 2.27 and 1.90 (adamantane H's), broad absorption due to NH between 7 and 8.

Anal. Calcd for $C_{11}H_{19}BrN_2S$: C, 45.36; H, 6.52; N, 9.62; S, 10.99. Found: C, 45.20; H, 6.50; N, 9.88; S, 11.06.

The salt (64.0 g) was stirred with 5% aqueous NaOH (400 ml) containing ethanol (100 ml) for 16 hr and the solution was acidified and extracted with ether–benzene to yield **12** (28 g, 76%): mp 102–104° (lit.[9] mp 100–102°); pmr ($CDCl_3$) two singlets showing fine splitting δ 2.05 and 1.75 (adamantane H's).

1-Ethylthioadamantane.—1-Adamantanethiol (5.04 g, 0.03 mol) was added to a stirred solution of sodium ethoxide (1.15 g of Na in 100 ml of absolute ethanol), followed by ethyl bromide (5.45 g, 0.05 mol). After 1 hr under reflux, solvents were evapo-

(5) D. N. Kevill and F. L. Weitl, *J. Amer. Chem. Soc.*, **90**, 6416 (1968).

(6) F. N. Stepanov and Y. I. Srebrodol'skii, *J. Org. Chem. USSR*, **2**, 1590 (1966).

(7) Melting and boiling points are uncorrected. Analyses were obtained by Micro-Tech Laboratories, Skokie, Ill. Analyses for N were performed by Mr. Richard Dvorak using a Model 20 Coleman nitrogen analyzer. Pmr spectra were obtained by means of a Varian A-60 instrument and are recorded in parts per million (δ) downfield from TMS.

(8) Purchased from Aldrich Chemical Co.

(9) J. R. Geigy, A. G. Belgian Patent 629,370 (Oct 21, 1963); *Chem. Abstr.*, **60**, 9167 (1964).

rated at 20 mm, and the residue was diluted with water and ether. Distillation produced the sulfide (3.65 g, 38%): bp 115–116° (0.02 mm); pmr (CCl_4) δ 2.50 (q, CH_2CH_3), 1.20 (t, CH_3), 2.27–1.60 (adamantane H's).

Anal. Calcd for $C_{12}H_{20}S$: C, 73.47; H, 10.20; S, 16.32. Found: C, 73.35; H, 10.24; S, 16.09.

1-Methylthioadamantane was synthesized in 88% yield in an analogous manner, bp 100–101° (0.01 mm) [lit.[10] bp ~70° (0.05 mm)].

β-(1-Adamantanethio)ethylamine.—1-Adamantanethiol (16.0 g, 0.1 mol) was added to sodium ethoxide solution (5.75 g of Na, 150 ml of ethanol), followed by 2-bromoethylamine hydrobromide (20.5 g, 0.1 mol). The mixture was stirred at 25° for 0.5 hr and then at the reflux for 4 hr. Solids were filtered off and the solvents evaporated *in vacuo*. The residue was diluted by water and extracted with ether–benzene (1:1), and the product was distilled (15.5 g, 77%): bp 144–148° (1.2 mm); pmr ($CDCl_3$) δ 3.08–2.48 (m, NCH_2CH_2S), 2.25–1.60 (adamantane H's). In dilute solution, a singlet at δ 1.5 was seen (NH_2).

Anal. Calcd for $C_{12}H_{21}NS$: C, 68.24; H, 9.95; N, 6.63; S, 15.16. Found: C, 68.01; H, 9.88; N, 6.48; S, 14.94.

The **hydrochloride** was prepared quantitatively in ether with HCl gas or in 75% yield when amine was added to cold concentrated HCl: mp 242–244°; pmr ($CDCl_3$) δ 3.5–2.8 (m, NCH_2-CH_2S), 2.25–1.60 (m, adamantane H's).

Anal. Calcd for $C_{12}H_{22}ClNS$: N, 5.66. Found: N, 5.52.

The amine (4.2 g) was treated with benzoyl chloride (2.8 g) in pyridine (5 ml) and benzene (50 ml) at 100° for 0.5 hr. The *benzamide* (4.6 g) was isolated in the usual fashion: mp 81–83° (from aqueous ethanol); pmr (CCl_4) δ 8.1–7.4 (arene H), 3.55 (m, CH_2N), 2.72 (t, CH_2S), 2.2–1.5 (adamantane H's).

Anal. Calcd for $C_{19}H_{25}NOS$: N, 4.44. Found: N, 4.49.

Reaction of the amine (1.05 g) with *p*-toluenesulfonyl chloride (1.14 g) in boiling pyridine (25 ml) for 1.5 hr afforded the **sulfonamide** (1.55 g), mp 86–88° (from ethanol).

Anal. Calcd for $C_{19}H_{27}NO_2S_2$: N, 3.83. Found: N, 3.69.

ε-(1-Adamantanethio)pentylamine.—1-Adamantanethiol (16.8 g) was added to sodium ethoxide solution (3.45 g of Na in 150 ml of ethanol), followed by δ-bromovaleronitrile[8] (16.2 g). After 3 hr at the reflux, the **sulfide nitrile** (25.2 g, mp 53–55°) was isolated as described for 1-ethylthioadamantane above.

A portion (15.56 g) was reduced by $LiAlH_4$ (5.7 g) in boiling ether (100 ml) over 2 hr. The reaction mixture was treated with water (40 ml) and **16** (10.3 g) was isolated from the ether extract, bp 182–186° (1.4 mm).

Anal. Calcd for $C_{15}H_{27}NS$: N, 5.72. Found: N, 5.53.

***N*-[β-(1-Adamantanethio)ethyl]chloroacetamidine Hydrochloride (19).**—To a stirred sodium methoxide solution (0.23 g of Na in 50 ml of methanol) was added chloroacetonitrile (7.5 g, 0.1 mol) in methanol (25 ml). After 0.5 hr, there was added β-(1-adamantanethio)ethylamine (16.77 g, 0.08 mol) in methanol (100 ml). The mixture was acidified by methanolic HCl to pH 4, stirred for 1 hr, filtered, and concentrated *in vacuo*. The product (17.2 g, 67%) was crystallized from 2-propanol–ether: mp 149–151°; pmr (CF_3CO_2H) δ 4.63 (s, CH_2Cl), 3.78 (m, CH_2N), 3.08 (t, CH_2S), 2.33–1.55 (m, adamantane H's).

Anal. Calcd for $C_{14}H_{24}Cl_2N_2S$: N, 8.66. Found: N, 8.63.

***S*-{*N*-[β-(1-Adamantanethio)ethyl]carboxamidiniummethyl} Thiosulfate (20).**—An aqueous solution of $Na_2S_2O_3 \cdot 5H_2O$ (10.0 g, 0.03 mol in 45 ml) was added to a solution of **19** (10.0 g, 0.03 mol) in methanol (150 ml). The mixture was stirred at 25° for 1.5 hr and then at 100° for 10 min. Solvents were removed *in vacuo*. The residue was diluted with water (20 ml) and recrystallized from ethanol–ether (1:4) to provide the product (8.35 g, 74%): mp 150–151°; pmr (CF_3CO_2H) δ 4.42 (s, $CH_2S_2O_3$), 3.75 (CH_2N), 3.67 (t, CH_2S) 2.46–1.65 (m, adamantane H's).

Anal. Calcd for $C_{14}H_{24}N_2S_3O_3$: C, 46.15; H, 6.59; N, 7.69; S, 26.37. Found: C, 45.82; H, 6.62; N, 7.66; S, 26.26.

***N*-[β-(1-Adamantanoxy)ethyl]chloroacetamidine Hydrochloride (8).**—This salt was prepared in 68% yield from β-(1-adamantanoxy)ethylamine[11] and chloroacetonitrile as described for the thio analog: mp 191–192° (from methanol–ether); pmr (CF_3CO_2H) δ 4.58 (s, CH_2Cl), 4.18 (m, CH_2O), 2.37–1.85 (m, adamantane H's).

Anal. Calcd for $C_{14}H_{24}Cl_2N_2O$: N, 9.15. Found: N, 9.31.

***S*-{*N*-[β-(1-Adamantanoxy)ethyl]carboxamidiniummethyl} Thiosulfate (9).**—Conversion of **8** to **9** was accomplished in 93% yield as described for the thio analog: mp 165; pmr (CF_3CO_2H) δ 4.70 (m, CH_2O), 3.97 (m, CH_2N), 3.80 (S, CH_2S), 2.40–1.67 (m, adamantane H's).

Anal. Calcd for $C_{14}H_{24}N_2O_4S_2$: C, 48.28; H, 6.99; N, 8.03; S, 18.39. Found: C, 48.54; H, 7.01; N, 7.94; S, 18.14.

***S*-{*N*-[β-1-(Adamantanoxy)propyl]carboximidiniummethyl} Thiosulfate (11)** was prepared in 21% yield directly from β-(1-adamantanoxy)propylamine[11] and chloroacetonitrile without the isolation of the intermediate chloroacetamidine by the method described previously.[12] It melted at 156–158°.

Anal. Calcd for $C_{15}H_{26}N_2O_4S_2$: C, 49.72; H, 7.18; N, 7.72; S, 17.68. Found: C, 49.99; H, 7.35; N, 7.69; S, 16.87.

***S*-{*N*-[γ-(1-Adamantanoxy)propyl]carboxamidiniummethyl} Thiosulfate (10)** was prepared from γ-(1-adamantanoxy)propylamine[11] in 38% yield: mp 170°; pmr (CF_3CO_2H) δ 4.67 (m, CH_2O), 4.50 (m, CH_2N), 3.78 (s, CH_2S), 2.5–1.67 (CH_2 and adamantane H's).

Anal. Calcd for $C_{15}H_{26}N_2O_4S_2$: C, 49.94; H, 7.18; N, 7.73; S, 17.68. Found: C, 49.63; H, 7.27; N, 7.50; S, 17.48.

Cleavage of Sulfides.—The general procedure is illustrated for β-(1-adamantanethio)ethylamine (**15**).

The **amine** (2.0 g) was heated with concentrated HCl (40 ml) under reflux for 3 hr. 1-Chloroadamantane (1.45 g, 90%) sublimed in part into the condenser and in part remained suspended in solution. It was recovered with ether and was identified by its mp 165–166° (lit.[4] mp), and mass and pmr spectrum.[13]

The aqueous solution was made alkaline with 10% NaOH solution and treated with benzoyl chloride (3.5 g) to give *S*-(β-benzamidoethyl) thiolbenzoate (1.9 g): mp 95–96.5° (from benzene) (lit.[14] mp 96–97°); pmr ($CDCl_3$) δ 8.6–7.5 (m, arene H), 7.2 (broad s, NH), 3.85 (m, CH_2N), 3.43 (m, CH_2S).

Similar hydrolysis of ε-(1-adamantanethio)pentylamine (2.0 g) with boiling concentrated HCl (40 ml) resulted in 1-chloroadamantane (83%). On basifying the aqueous solution and addition of benzoyl chloride, there was isolated *S*-(ε-benzamidopentyl) thiolbenzoate (2.3 g): mp 72–75° (from benzene); pmr ($CDCl_3$) δ 8.4–7.4 (m, arene H), 6.8 (broad s, NH), 3.52 (m, CH_2N), 3.17 (m, CH_2S), 1.61 (broad s, three CH_2).

Anal. Calcd for $C_{19}H_{21}NO_2S$: N, 4.28. Found: N, 4.22.

Registry No.—**8**, 30771-83-6; **9**, 30771-84-7; **10**, 30771-85-8; **11**, 30771-86-9; **14**, 17233-15-7; **15**, 30771-87-0; **15** HCl, 30771-88-1; **16**, 30771-89-2; **17**, 30771-90-5; **18**, 30771-91-6; **19**, 30771-92-7; **20**, 30771-93-8; **21**, 30771-94-9; 5-(1-adamantanethio)-pentylnitrile, 30771-95-0; *S*-(ε-benzamidopentyl) thiolbenzoate, 30771-96-1.

(10) D. R. Rayner, A. J. Gordon, and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4854 (1968).

(11) J. K. Chakrabarti, M. J. Foulis, and S. S. Szinai, *Tetrahedron Lett.*, 6249 (1968).

(12) A. P. Parulkar and L. Bauer, *J. Heterocycl. Chem.*, **3**, 472 (1966); J. M. Barton and L. Bauer, *Can. J. Chem.*, **47**, 1233 (1969).

(13) Identical with that reported by R. C. Fort, Jr., and P. v. R. Schleyer, *J. Org. Chem.*, **30**, 789 (1965).

(14) C. J. M. Stirling, *J. Chem. Soc.*, 4524 (1958).