out to give **4e**: 389 mg (89% yield); mp 85 °C (lit.[21] mp 85–86 °C).

2-Thienylacetic Acid (4f). By use of the same procedure, the hydrolysis of **3f** (666 mg, 2.77 mmol) was carried out to give **4f**: 326 mg (83% yield); mp 74–75 °C (lit.[22] mp 76 °C).

1-Naphthylacetic Acid (4g). By use of the same procedure, the hydrolysis of **3g** (506 mg, 1.779 mmol) was carried out to give **4g**: 317 mg (96% yield); mp 131–132.5 °C (lit.[23] mp 131 °C).

Registry No. 1, 36602-08-1; (*E*)-**3a**, 86803-42-1; (*Z*)-**3a**, 86803-49-8; (*E*)-**3b**, 86803-43-2; (*Z*)-**3b**, 86803-50-1; **3c**, 86803-44-3; (*E*)-**3d**, 86803-45-4; (*Z*)-**3d**, 86803-51-2; (*E*)-**3e**, 86803-47-6; (*Z*)-**3e**, 86803-53-4; (*E*)-**3f**, 86803-46-5; (*Z*)-**3f**, 86803-52-3; (*E*)-**3g**, 86803-48-7; (*Z*)-**3g**, 86803-54-5; **4a**, 109-52-4; **4b**, 111-14-8; **4c**, 117-34-0; **4d**, 103-82-2; **4e**, 104-01-8; **4f**, 1918-77-0; **4g**, 86-87-3; *n*-C_3H_7CHO, 123-72-8; *n*-$C_5H_{11}CHO$, 66-25-1; $Ph_2C{=}O$, 119-61-9; PhCHO, 100-52-7; *p*-$(CH_3O)C_6H_4CHO$, 123-11-5; 2-thiophenecarboxaldehyde, 98-03-3; 1-naphthalenecarboxaldehyde, 66-77-3.

(21) R. Pschorr, O. Wolfes, and W. Buckow, *Chem. Ber.*, **33**, 172 (1900).
(22) F. Ernst, *Chem. Ber.*, **19**, 3281 (1886).
(23) P. Boessneck, *Chem. Ber.*, **16**, 641 (1883).

Reactions of 2-*anti*-Hydroxy-4-aza-5-homoadamantan-5-one

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In a previous publication[1] we reported on rearrangement reactions of three different kinds of oxahomoadamantanes (**1–3**, Chart I). We had found that each derivative followed a different reaction pathway when exposed to concentrated mineral acids (H_2SO_4, HCl or HBr) and postulated a common epoxonium ion, **4**, as intermediate. In concentrated hydriodic acid, however, the oxahomoadamantanes **1–3** were reduced, and only iodoadamantanes could be isolated.[1]

In continuation of this work we performed analogous reactions using 2-*anti*-hydroxy-4-aza-5-homoadamantan-5-one (**5**) as the starting material.[2] Our purpose was to determine whether products were formed which indicate that an aziridinium ion, **6**, may have been formed during the reaction in analogy to the lactone.

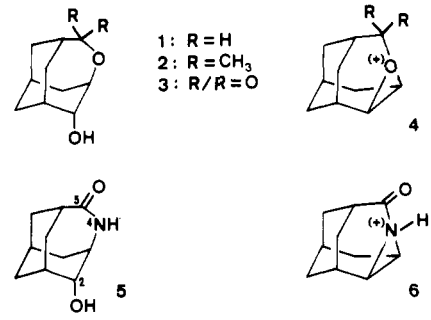
Results and Discussion

The hydroxy lactam **5** was refluxed in 36% hydrochloric, 48% hydrobromic, and 57% hydriodic acid, respectively, for 18 h, and the products isolated, after the workup and chromatographic separation, are listed in Chart II (the values in parentheses indicate the yields of isolated material).

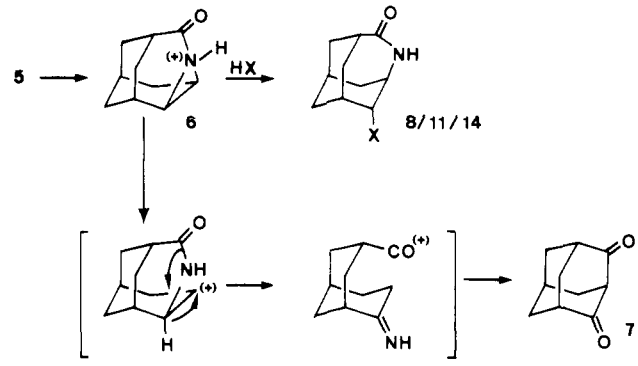
A variety of compounds were produced in contrast to the corresponding reactions[1] of the lactone **3** which furnished the diketone **7** as the sole isolable product in H_2SO_4 and HBr and a mixture of **15** and **16** in HI. In each case with **5**, small but detectable amounts of **7** were found as well as the halo lactams **8**, **11**, and **14** which were generated in increasing yields when going from Cl to Br and I. A comparison of these findings with the results of the lactone reactions (cf. Schemes IV and III in ref. 1) strongly suggests that the aziridinium ion **6** is involved as an intermediate which is either attacked regio and stereoselectively (probably due to steric reasons; cf. ref 1) by an halide anion to form **8**, **11**, or **14**, respectively, or undergoes a rearrangement[1,3] to **7** via an easily hydrolizable imine (Scheme I).

The reduction to iodoadamantanes (cf. Scheme VI in ref 1) is now retarded considerably. This is explicable on the basis of the reduction mechanism proposed for **3**[1] (Scheme II).

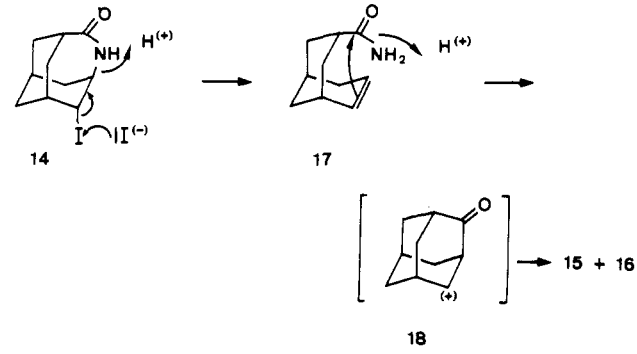
Chart I



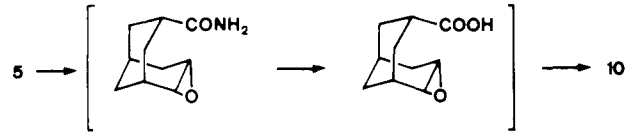
Scheme I



Scheme II



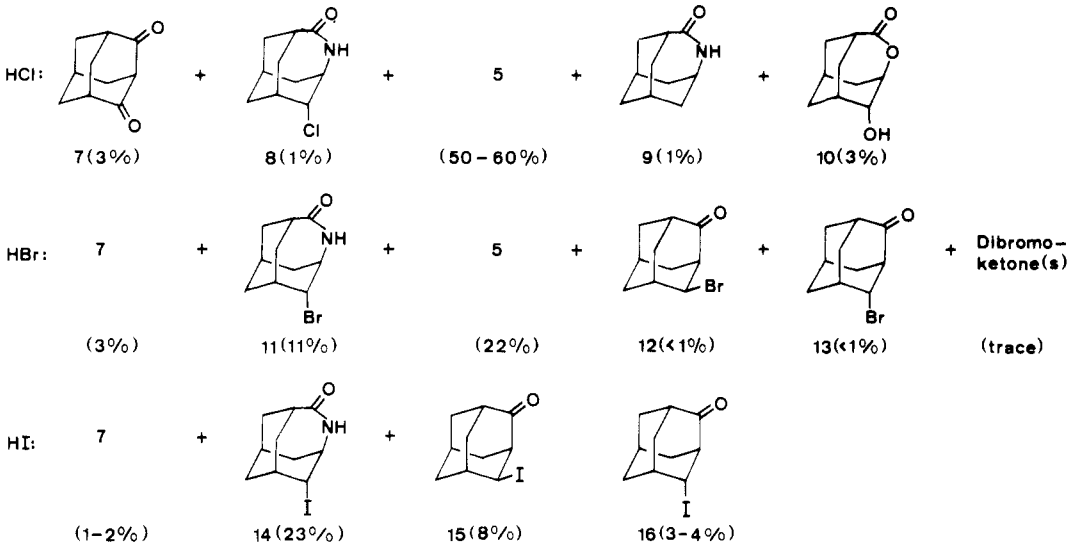
Scheme III



(1) Duddeck, H.; Wiskamp, V.; Rosenbaum, D. *J. Org. Chem.* **1981**, *46*, 5332.
(2) Hassner, A.; Morgan, T. K., Jr.; McLaughin, A. R. *J. Org. Chem.* **1979**, *44*, 1999.
(3) Blackett, B. N.; Coxon, J. M.; Hartshorn, M. P.; Richards, K. E. *Aust. J. Chem.* **1970**, *23*, 839, 2077; *J. Am. Chem. Soc.* **1970**, *92*, 2574. For a survey see: (a) Rosowsky, A. "Heterocyclic Compounds with Three- and Four-Membered Rings"; Weissenberger, A., Ed.; Wiley-Interscience: New York, 1964; Vol. 19, Part 1. (b) Paquette, L. A. *MTP Int. Rev. Sci.: Org. Chem., Ser. One* **1973**, *5*, 127.

0022-3263/83/1948-3569$01.50/0

Chart II



The tendency for cleavage and ring closure to the adamantane skeleton (**14** → **17** → **18**) was expected to be clearly less pronounced in the aza than in the oxa derivative. In HBr, reduction occurs only on a very small scale. Surprisingly, however, a trace constituent was detected which seems to be a dibromoadamantanone or a mixture of such isomers on the basis of mass spectral data. The structure of this sample has not been established and is currently under investigation. The HCl reaction afforded two more products in small amounts, namely, the unsubstituted lactam **9** and the hydroxy lactone **10**. Whereas no reasonable mechanism can be offered presently for the former, the latter compound may be produced by hydrolysis of an intermediate epoxy amide (Scheme III).

We could not detect compound **10**, however, when using HBr and HI. At least in the HI case this is not astonishing, since **10** is readily converted to **15** and **16** under these conditions.[1] There is a considerable loss of material in all reactions, and despite a painstaking search, we could not find traces of any other compounds in the residue. Thus, we believe that the weight loss is due to the formation of degradation products which are highly soluble in water.

In conclusion, the results depicted in Chart II suggest that the stereoselective substitution reactions (**5** → **8**, **11**, and **14**, respectively) proceed via an intermediate aziridinium ion, **6**. Furthermore, **6** is capable of undergoing an aziridinium–imine rearrangement.[3] Reduction of **5** by HI is severely restrained in comparison with the analogous reaction of **3**. These findings support the reaction mechanisms proposed by us for the corresponding oxahomoadamantanes.[1]

Experimental Section

Melting points were determined on a Büchi-Tottoli melting point apparatus and are uncorrected. Infrared spectra were recorded on a Shimadzu IR-400 spectrophotometer, and ^{1}H NMR spectra were obtained on Varian T-60 or Bruker WP-80 spectrometers with deuterated chloroform as the solvent. The chemical shifts are referenced to internal tetramethylsilane. Mass spectra were recorded on Varian CH-5 and 731 spectrometers.

All compounds were purified by column chromatography on silica gel with various ligroin/acetone mixtures as eluants and were >98% pure. Compounds already known in literature (**5**,[2] **7**,[1,4,5] **9**,[6] **10**,[1] **12**,[7] **13**,[7] **15**,[7b] and **16**[7b]) were identified by comparison with their published spectra. Except for **5**, authentic samples were available for comparison by thin-layer chromatography and by their ^{1}H NMR spectra. All reported yields refer to isolated samples after purification and are not optimized but are reproducible.

General Synthetic Procedure. 2-*anti*-Hydroxy-4-aza-5-homoadamantan-5-one (**5**, 500 mg) was refluxed in 50 mL of concentrated aqueous HX (X = Cl, Br, or I) for 18 h. After the mixture cooled, 50 mL water was added, and the mixture was extracted four times with methylene chloride (50 mL/extraction). The combined organic layers were washed with sodium bisulfite, sodium bicarbonate, and water successively. After the mixture was dried over anhydrous sodium sulfate, it was evaporated. The resulting crude mixtures were separated by column chromatography. Unreacted **5** could be recovered from the aqueous layer by adding sodium hydroxide until alkaline and sodium chloride until a saturated solution was obtained. This mixture was extracted three times with chloroform, and the organic layer was worked up as described above.

2-*anti*-Chloro-4-aza-5-homoadamantan-5-one (8): yield ca. 1% as a white solid; IR ($CHCl_3$) 3600–3100 (NH), 2900, 1645 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.67–6.17 (1 H, br s, NH), 4.22 (1 H, m, CHCl), 3.36 (1 H, m, C*H*NH), 2.70 (1 H, m, CHCO), 2.57–1.33 (10 H, m); mass spectrum, *m/e* (relative intensity) 201/199 (15/46), 164 (100), 136 (76), 79 (55); molecular weight by high-resolution mass spectrometry, calcd for $C_{10}H_{14}ClNO$ 199.0761/201.0731, found 199.0776/201.0746.

2-*anti*-Bromo-4-aza-5-homoadamantan-5-one (11): yield 11% as a white solid; mp 190–191 °C; IR ($CHCl_3$) 3600–3150 (NH), 2900, 1645 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.64–7.12 (1 H, br s, NH), 4.39 (1 H, m, CHBr), 3.51 (1 H, m, C*H*NH), 2.62 (1 H, m, CHCO), 2.51–1.30 (10 H, m); mass spectrum, *m/e* (relative intensity) 245/243 (21/21), 164 (100), 79 (42). Anal. Calcd for $C_{10}H_{14}BrNO$: C, 49.20; H, 5.78; N, 5.74. Found: C, 49.45; H, 5.80; N, 6.20.

2-*anti*-Iodo-4-aza-5-homoadamantan-5-one (14): yield 23% as a white solid; mp 194–195 °C; IR ($CHCl_3$) 3600–3150 (NH), 2900, 1645 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.55–7.01 (1 H, br s, NH), 4.60 (1 H, m, CHI), 3.50 (1 H, m, C*H*NH), 2.60 (1 H, m, CHCO), 2.44–1.35 (10 H, m); mass spectrum, *m/e* (relative intensity) 291 (<1), 164 (100), 121 (30), 79 (31). Anal. Calcd for $C_{10}H_{14}INO$: C, 41.25; H, 4.85; N, 4.81. Found: C, 41.00; H, 4.90; N, 5.30.

^{13}C NMR spectra of all compounds have been recorded. They corroborate the given structures and will be published in a forthcoming paper.

(4) Faulkner, D.; McKervey, M. A. *J. Chem. Soc. C* **1971**, 3906 and references therein.

(5) McKervey, M. A.; Faulkner, D.; Hamill, H. *Tetrahedron Lett.* **1970**, 1971.

(6) Sasaki, T.; Eguchi, S.; Toru, T. *J. Org. Chem.* **1970**, *35*, 4109.

(7) (a) Duddeck, H. *Org. Magn. Reson.* **1975**, *7*, 151. (b) Duddeck, H.; Wolff, P. *Ibid.* **1977**, *9*, 528. (c) Vodička, L.; Třiska, J.; Hájek, M. *Collect. Czech. Chem. Commun.* **1980**, *45*, 2670.

Acknowledgment. We acknowledge generous support from the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Registry No. 5, 69631-77-2; 7, 19214-00-7; 8, 86729-16-0; 9, 22607-75-6; 10, 79499-77-7; 11, 86729-17-1; 12, 32456-48-7; 13, 32456-49-8; 14, 86729-18-2; 15, 56781-86-3; 16, 56781-85-2; HCl, 7647-01-0; HBr, 10035-10-6; HI, 10034-85-2.

Facile Syntheses of Aldehydes and β-Dialdehyde Monoacetals

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During recent research on the synthesis of β-lactam antibiotics, our synthetic strategy required the preparation of 2,2-dimethyl-1,3-propanedial (1 Chart I) with one of the aldehydes suitably masked. Either the β-dialdehyde monoacetal **2a**, β-dialdehyde monothioacetal **2b**, or the other masked aldehyde **2c** where Y could be readily converted to the aldehyde function would serve the synthetic purpose.

The unsubstituted β-dialdehyde monothioacetal **3** has been prepared by the displacement of bromoacetaldehyde diethyl acetal by 2-lithio-1,3-dithiane followed by acid hydrolysis.[1] We anticipated that this would not be preparatively useful to synthesize **2b** since it involved an S_N2 substitution reaction of a tertiary bromide. Trimethylsilyl enol ethers, in the presence of $TiCl_4$ and orthoformate, are known to generate β-keto acetals.[2] However, no example has been given for the preparation of a β-dialdehyde monoacetal. Reaction of the trimethylsilyl enol ether **4** with trimethyl orthoformate in the presence of $TiCl_4$ gave the desired β-dialdehyde derivative **2d** in less than 5% yield.[3]

Methyl Phenyl Sulfides as Masked Aldehydes. Methyl phenyl sulfides have been used as aldehyde synthons.[4] However, the experimental procedure for the generation of the aldehyde requires strong base or mercury-mediated cleavage over a lengthy period. This procedure precludes their use as aldehyde equivalents in sensitive molecules such as β-lactams. This problem obviously limits the usefulness of utilizing methyl phenyl sulfides as an aldehyde synthon.

In searching for a practical synthesis of the β-dialdehyde derivative, we discovered a mild and convenient procedure for converting methyl phenyl sulfide to the aldehyde group. In this paper we report this procedure that may extend the synthetic utility of this group in the preparation of aldehydes of sensitive molecules and other β-dialdehyde derivatives.

The rationale which led to this procedure was based on the hypothesis that sulfuryl chloride readily α chlorinates methyl phenyl sulfide to yield the chloromethyl phenyl sulfide derivative **6**, which upon treatment with water in the presence of silica gel would give hydroxy intermediate

Chart I[a]

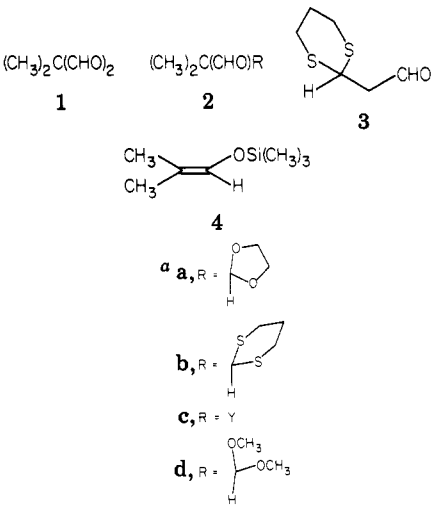
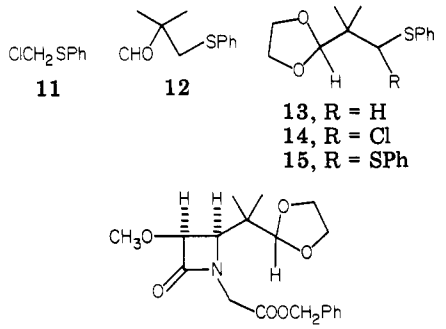
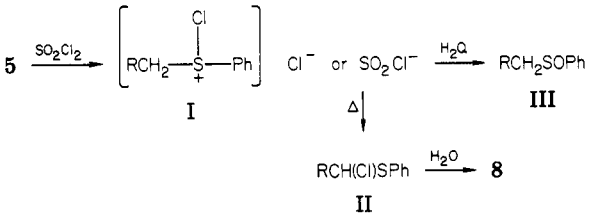


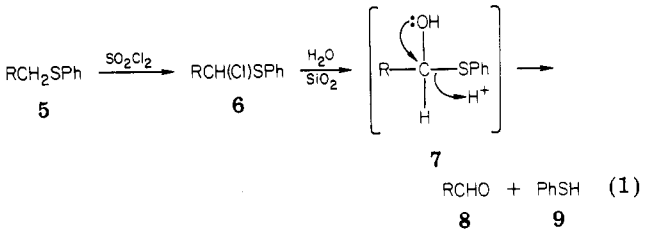
Chart II



Scheme I



7, which would fragment to yield the aldehyde **8** and thiophenyl **9** (eq 1).



Oxidation of sulfides to sulfoxides by the use of sulfuryl chloride in the presence of wet silica gel had recently been reported by Hojo et al.[5] Our experimental technique, however, has yielded predominantly the aldehyde. Hojo's procedure involved water, SiO_2, sulfuryl chloride, and sulfide in the same reaction medium while our procedure allowed sulfuryl chloride to react with the sulfides to form the α-chloro sulfides first before addition to the water-deactivated silica gel columns. The difference of reaction courses may be explained by the mechanistic consideration

(1) Trost, Barry M.; Kunz, Robert A. *J. Am. Chem. Soc.* **1975**, *97*, 7152.
(2) Mukaiyama, Teruaki; Hayashi, Masatoshi. *Chem. Lett.* **1974**, 15.
(3) The presence of **2d** was detected NMR upon enriching the product by repeated purification on silica gel column.
(4) Paquette, Leo A.; Klobucar, W. D.; Snow, Robert A. *Synth. Commun.* **1976**, *6*, 575.
(5) Hojo, Masaru; Masuda, Ryoichi. *Tetrahedron Lett.* **1976**, 613.

0022-3263/83/1948-3571$01.50/0