duction in unspecified yield (product isolated as oxazolidine) of 3(β),17(β)-diacetoxy-17-iso-$\Delta^{5,6}$-etiocholenic acid nitrile with lithium aluminum hydride in ether. Amundsen and Nelson[6] found that maximum yields of amines from nitriles were obtained when the molar ratio of hydride to nitrile was one to one, lower yields being obtained when less hydride was used.

In the reduction reported here, the use of one and a half moles of hydride to one of cyanohydrin gave yields of 62–67%, and increasing the amount of hydride to two moles increased the yield to 76%. The method is convenient and requires no special equipment, and should prove to be a useful synthetic method for the preparation of aminoalcohols from cyanohydrins.

Experimental

1-Aminomethyl-cyclohexanol.—Cyclohexanone cyanohydrin was prepared from potassium cyanide and the bisulfite addition product of cyclohexanone according to the method of Tchoubar.[2b] Using 150 g. (1.53 moles) of cyclohexanone, the cyanohydrin (b.p. 112–115° (11 mm.)) was obtained in 70–79% yield.

A solution of 125 g. (1.0 mole) of cyclohexanone cyanohydrin in 200 ml. of absolute alcohol-free ether was added dropwise over a period of one hour to a well stirred slurry of 76 g. (2.0 moles) of lithium aluminum hydride (Metal Hydrides, Inc.) in 2 liters of ether in a three-necked, 5-liter flask (cooled in an ice-bath throughout the addition) fitted with an efficient reflux condenser, dropping funnel, and mercury-sealed Hershberg stirrer. After the addition, the mixture was stirred overnight at room temperature, and then the addition complex was decomposed by adding dropwise 50 ml. of water, 40 ml. of 20% sodium hydroxide solution, and finally 150 ml. of water. The resulting mixture was filtered, the filtrate dried over anhydrous sodium sulfate, the ether removed, and the residue distilled to yield 69 g. (53.5%) of 1-aminomethylcyclohexanol, b.p. 95–115° (22 mm.) (major portion 110–115°). The filter cake was digested with 600 ml. of hot benzene, and the benzene solution was dried and distilled to yield an additional 28.7 g. of aminoalcohol, b.p. 93–115° (20 mm.), total yield 97.7 g. (75.5%). The hydrochloride melted at 214.5–215.5° dec. (cor.) (reported[2] 215–216°) and the picrate at 169.5–171° (cor.) (reported[2] 168–170°).

The infrared spectra of the aminoalcohol prepared by the above method agreed in every respect with that of a sample of 1-aminomethylcyclohexanol prepared by the hydrogenation of cyclohexanone cyanohydrin. The strong band at 1700 cm.$^{-1}$ (unassigned) and the medium band at 2232 cm.$^{-1}$ (C≡N) of the cyanohydrin were absent in the aminoalcohol prepared above, thus assuring its purity. All spectra were taken on a modified Perkin-Elmer Model 12B infrared spectrometer in which a double beam rearrangement replaced the original single beam optical system.[7] Samples of the pure liquid were compressed between sodium chloride windows. A calcium fluoride prism was used.

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Comparative Ease of Cleavage of Some Phenyl Alkyl and Phenyl Aralkyl Sulfides

BY D. S. TARBELL AND DONALD P. HARNISH[1]

The present study was undertaken to find out how the ease of cleavage of the carbon–sulfur bond varies, in a series of phenyl alkyl and phenyl aralkyl sulfides, with the structure of the sulfide, and to obtain data for a comparison of the corresponding sulfur and oxygen compounds.[2]

The behavior of the sulfides listed in the table was examined toward a variety of agents of varying degrees of effectiveness; the results with aluminum bromide in chlorobenzene and with aqueous hydrobromic acid, which allow the most general comparison of activity, are tabulated. It is clear that, as would be expected, the rate of cleavage of the sulfides, C_6H_5SR, to form C_6H_5SH, follows the order $(C_6H_5)_3C > (C_6H_5)_2CH > C_6H_5CH_2 > C_6H_5CH_2CH_2$. This order is emphasized by further observations that $C_6H_5SC(C_6H_5)_3$ is converted by alcoholic iodine (even at room temperature) to triphenylcarbinol, diphenyl disulfide and ethyl trityl ether, but $C_6H_5SCH(C_6H_5)_2$ is unaffected by this reagent, even on boiling. The trityl sulfide is cleaved by aluminum bromide in ether or nitrobenzene, which, being strong donor solvents, completely prevent cleavage of benzyl phenyl sulfide by aluminum bromide.[2a] The trityl and benzhydryl sulfides are both cleaved by alcoholic silver nitrate.[3]

The slower rate of cleavage of sulfides in comparison with the corresponding ethers, is shown by the rapid splitting of benzyl phenyl ether by hydrogen bromide in acetic acid at room temperature,[4] and by the splitting of phenyl trityl ether by hydrogen chloride in acetic acid in the cold.[5] The deactivating effect toward electrophilic substitution in an aromatic ring of sulfur, compared to oxygen,[2d] is indicated by the isolation, after iodine oxidation of the reaction mixture, of diphenyl disulfide from the aluminum bromide catalyzed cleavage of the benzyl, benzhydryl and trityl phenyl sulfides; the analogous oxygen compounds give much nuclear alkylation under comparable conditions.[2a,6]

In the series C_6H_5SR, the ease of cleavage follows the expected order[7] $C(CH_3)_3 > CH(CH_3)_2 > CH_3$. *t*-Butyl phenyl sulfide is not, however, affected by alcoholic iodine or alcoholic silver nitrate, in contrast to the benzhydryl and trityl compounds. The thermal[8] and aluminum chloride[8,9] catalyzed cleavage of $C_6H_5OC(CH_3)_3$ lead to *p*-*t*-butylphenol, and the action of boron fluoride on isopropyl aryl ethers leads to isopropylphenols[10]; these carbon–oxygen cleavages appear to take place far more rapidly than the carbon–sulfur cleavages listed in the table. In agreement with this, it has been found[11] that ani-

(1) Beaunit Mills Fellow, 1947–1948.

(2) Preceding papers on this topic: (a) D. P. Harnish and D. S. Tarbell, THIS JOURNAL, **70**, 4123 (1948); (b) *Anal. Chem.*, **21**, 968 (1949); (c) H. F. Wilson and D. S. Tarbell, THIS JOURNAL, **72**, 5200 (1950); (d) D. S. Tarbell and J. C. Petropoulos, *ibid.*, **74**, 244 (1952); (e) D. S. Tarbell and D. P. Harnish, *Chem. Revs.*, **49**, 1 (1951).

(3) D. C. Gregg, H. A. Iddles and P. W. Stearns (*J. Org. Chem.*, **16**, 246 (1951)) found that phenyl trityl sulfide was cleaved by methanolic mercuric chloride at room temperature.

(4) B. W. Tronow and L. W. Ladigina, *Ber.*, **62**, 2844 (1929).

(5) A. Baeyer, *ibid.*, **42**, 2626 (1909).

(6) H. A. Iddles, *et al.*, THIS JOURNAL, **62**, 2757 (1940); **64**, 3154 (1942); J. Van Alphen, *Rec. trav. chim.*, **46**, 287, 803 (1927).

(7) J. F. Norris and G. W. Rigby, THIS JOURNAL, **54**, 2088 (1932), showed that the rates of cleavage of ethyl butyl ethers by concentrated hydrochloric acid followed the order *t*-butyl > *s*-butyl > *n*-butyl.

(8) R. A. Smith, *ibid.*, **55**, 3718 (1933).

(9) T. W. Evans and K. R. Edlund, *Ind. Eng. Chem.*, **28**, 1188 (1936).

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(11) J. C. Petropoulos, unpublished observation.

sole is split completely to phenol by aluminum bromide in chlorobenzene after 18 hours at 60° (for the sulfur analog, see Table).

During this work several new aryl sulfides were prepared, which are described in the experimental part. It was found, however, that aluminum bromide caused hydrogen sulfide evolution from *p*-thiocresol, β-thionaphthol, and 4-phenylthiophenol, and hence kinetic runs could not be made on sulfides derived from these thiols. It was shown that aluminum bromide in chlorobenzene solution formed biphenyl from 4-phenylthiophenol.

$$p\text{-}C_6H_5C_6H_4SH \xrightarrow[C_6H_5Cl]{AlBr_3} C_6H_5C_6H_5$$

In benzene solution the products appeared to be biphenyl and diphenyl sulfide.

The carboxy sulfides in the table were found to be unaffected even by aluminum bromide–acetyl bromide, a combination which gives very rapid cleavage of benzyl phenyl sulfide.[2a]

Experimental[12]

The amount of cleavage was determined by the consumption of 0.02 *N* alcoholic iodine solution either directly as mercaptan or after hydrolysis of the thiol ester.[2b]

The sulfides below were prepared in the usual manner by adding alkyl halide to a solution of the thiophenol in alcoholic potassium hydroxide.

Sulfide	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
4-Biphenylyl benzyl sulfide[a]					
p-$C_6H_5C_6H_4SCH_2C_6H_5$	127.5–128.5	82.56	82.18	5.83	5.77
4-Biphenylyl ethyl sufide					
p-$C_6H_5C_6H_4SCH_2CH_3$	74–75	78.46	78.20	6.58	6.56
β-Naphthyl benzyl sulfide					
β-$C_{10}H_7SCH_2C_6H_5$	88.5–89	81.56	81.33	5.64	5.76

[a] The sulfoxide was prepared from the reaction of bromine water on a solution of the sulfide in *t*-butyl alcohol[2b]; m.p. 198–199°. Calcd. for $C_{19}H_{16}OS$: C, 78.05; H, 5.51. Found: C, 77.84; H, 5.40.

CLEAVAGE OF SULFIDES, C_6H_5SR

R	$AlBr_3$[a] Time, hr.	$AlBr_3$[a] Cleavage, %	HBr[b,c,d] Time, hr.	HBr[b,c,d] Temp., °C.	HBr[b,c,d] Cleavage, %
$C_6H_5CH_2$	5	85	6[b]	200	Decomp.
	73(0°)	42	24[c]	150	30
$C_6H_5CH_2CH_3$	18	0			
	2(79°)	10–20			
$(C_6H_5)_2CH$	0.2	86[e]	4[d]	Reflux	0
	0.2(0°)	64	0.2[c]	Reflux	10–20
$(C_6H_5)_3C$	18	≫50[e]	0.02[b]	Reflux	>5
	0.2(0°)	>50	1[h]	Reflux	>5
CH_3	24	0[h]			
	24(93°)	0			
$(CH_3)_2CH$	18	0[f]			
	6(72°)	5–10			
$(CH_3)_3C$	0.2	5–10			
CH_2COOH	4(50°)	0[g]			
	0.2(reflux)	0			
CH_2CH_2COOH	4(50°)	0			
	0.2(reflux)	0			

[a] Chlorobenzene as solvent; 28° unless otherwise stated. [b] 32% aqueous solution. [c] 32% solution in acetic acid. [d] 48% aqueous solution. [e] Diphenyl disulfide isolated from the reaction. [f] $AlBr_3$ without solvent gave 50–60% cleavage after 24 hours at 28°. [g] No cleavage when fused with $AlBr_3$ in absence of solvent. [h] Dilute aqueous hydrochloric acid.

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(12) Analyses by Mrs. G. Sauvage; melting points are corrected.

Arsenicals Containing Quinoline and Quinazoline Nuclei

BY YAO-HUA WU AND CLIFF S. HAMILTON

For a number of years various workers in this Laboratory have been employing the Bart reaction[1] to prepare different aromatic and heterocyclic arsonic acids as possible therapeutic agents. This reaction has now been utilized to synthesize 4-hydroxyquinoline- and 4-hydroxyquinazolinearsonic acids.

6-Amino-4-hydroxyquinoline, 6-amino-4-hydroxy-2-methyl-quinoline, 5-amino-4-hydroxyquinazoline, 6-amino-4-hydroxyquinazoline and 7-amino-4-hydroxyquinazoline were prepared by the reduction of the corresponding nitro compounds. The arsonic acids were obtained by diazotizing these amines and subsequent coupling with sodium arsenite. Some of these arsonic acids were reduced to their arsenoso derivatives by the action of sulfur dioxide and hydriodic acid.

The condensation of heterocyclic compounds containing an "active" halogen with aminoarylarsonic acids has been studied extensively by Banks and co-workers[2] and Hamilton and co-workers.[3] In most cases an aqueous suspension containing a trace of hydrochloric acid was used. Banks[2] pointed out that the trace of hydrochloric acid is necessary because the reaction rate in aqueous solution or suspension is increased by an increase in the hydrogen ion concentration. Because of the instability of the 4-haloquinolines and 4-haloquinazolines in aqueous acid solutions, the condensation with *p*-arsanilic acid was accomplished in N-dimethylformamide as a solvent.

Experimental

6-Amino-4-hydroxyquinolines.—6-Amino-4-hydroxyquinoline was prepared according to the direction of Albert, Brown and Duewell.[4] 6-Amino-4-hydroxy-2-methylquinoline was obtained by the method of Kermack and Weatherhead.[5]

Amino-4-hydroxyquinazolines.—The 4-hydroxynitroquinazoline (3.8 g.) was added gradually in portions to a warm solution of stannous chloride ($SnCl_2 \cdot 2H_2O$, 20.3 g.) in concd. hydrochloric acid (30 ml.). After all the solid had been added, the solution was heated gently under reflux for 1 hour. The hot solution was diluted with water and care-

TABLE I

Compound	Yield, %	M.p., °C. Liter.	M.p., °C. Found
5-Amino-4-hydroxyquinazoline	76.4	235–236[6]	236
6-Amino-4-hydroxyquinazoline	67.0	318[7]	316
7-Amino-4-hydroxyquinazoline[a]	53.7	.....	315

[a] *Anal.* Calcd. for $C_8H_7ON_3$: C, 59.61; H, 4.38; N, 26.07. Found: C, 59.86; H. 4.25; N, 25.98.

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