TABLE IV

PHYSICAL PROPERTIES OF HYDROGENATED REACTION PRODUCTS AND CORRESPONDING DIACETAMIDO DERIVATIVES

Compound	B.p., °C.	Mm.	$n^{25}D$	Diacetamido deriv. m.p. (cor.), °C.	Analysis of diacetamido deriv., % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1-Phenylhexane	118	18	1.4839	203–204	69.53	8.75	...	69.33	8.79	...
3-Phenylhexane	83	18	1.4849	205–206	69.53	8.75	10.14	69.57	9.03	10.16
1-Phenylheptane	85	3	1.4835	196–197	70.31	9.02	9.65	69.91	9.33	9.59
3-Phenylheptane	100	18	1.4832	164–165	70.31	9.02	9.65	70.49	9.44	...
1-Phenyl-4-methylhexane	85–86	3	1.4838	197–198	70.31	9.02	9.65	70.61	9.40	9.53
3-Phenyl-4-methylhexane	95	12	1.4898	194–195	70.31	9.02	9.65	70.55	9.35	9.56

evaporation of ammonia the residue was diluted with benzene and filtered to remove the salt. The filtrate was stripped of solvent in a short column and the residue (78.6 g.) carefully distilled in the Podbielniak column under the same conditions as described under Method A. The results are given in Table III under Method B. Ultraviolet spectra were taken of several fractions to confirm the presence of conjugated olefins, *cis*- and *trans*-1-phenyl-1-butene. The refractive indexes of these fractions approach closely the most recent values[11] ($n^{25}D$ 1.5314 and 1.5382) for these olefins.

The distillation residues were treated in the same manner as in Method A and were identical. Molecular weight determination on the dimer by bromine titration gave 231 (calculated 236). Ultraviolet absorption spectra showed the following maxima (with shoulder at 283 mμ).

Molar extinction coefficient	Wave length, mμ
5450	249
240	292.5

(11) D. L. Hagmann, Ph.D. Thesis, University of California at Los Angeles, 1950.

Anal. Calcd. for $C_{18}H_{20}$: C, 91.47; H, 8.53. Found: C, 91.03; H, 8.54.

Dimethylation of Allylbenzene.—Fifty grams of allylbenzene (0.42 mole) was added to a solution of one mole of sodamide in 1.5 l. of liquid ammonia. Methyl bromide was distilled into the mixture until the color was completely discharged. The solvent was evaporated and organic material was taken up in benzene, the benzene solution washed with dilute sulfuric acid, dried and distilled through a column packed with platinum gauze, which had been described previously.[6] The distillation yielded 53% of α,α-dimethylallylbenzene, b.p. 188° (760 mm.), $n^{25}D$ 1.5085, d^{20}_4 0.9039; MR_D calcd., 48.93; found, 49.12,

Anal. Calcd. for $C_{11}H_{14}$: C, 90.35; H, 9.65. Found: C, 90.24; H, 9.7.

A second product, b.p. 197° (760 mm.), $n^{25}D$ 1.5252, was obtained in 3% yield. It gave on ozonization, acetophenone (identified as its 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 248°) and propionaldehyde (identified as its methone derivative[12]). This indicates the formation of some mixed primary–secondary-type of addition, with the formation of $C_6H_5C(CH_3)=CHCH_2CH_3$.

(12) E. C. Horning and M. G. Horning, *J. Org. Chem.*, **11**, 95 (1946).

LOS ANGELES 24, CALIFORNIA RECEIVED JULY 10, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Sulfonic Acid Esters of Aminoalcohols

BY ARTHUR C. COPE AND MARION BURG[1]

A number of esters of aliphatic and aromatic sulfonic acids and aminoalcohols containing secondary or tertiary amino groups have been prepared (and isolated as hydrochlorides) by reaction of the aminoalcohols, their hydrochlorides or sodium aminoalkoxides with sulfonyl chlorides at low temperatures. Chemical and pharmacological properties of the esters are reported.

Since many carboxylic acid esters of aminoalcohols have local anesthetic and other pharmacological activity, we were interested in studying sulfonic acid esters of aminoalcohols, which might differ in pharmacological properties because of their chemical dissimilarities. Sulfonic acid esters, for example, differ from carboxylic acid esters in rate and manner of hydrolysis, and are much more reactive alkylating agents.

A few sulfonic acid esters of aminoalcohols are mentioned in the patent literature, without details of methods of preparation or properties.[2] The preparation of 2-dimethylaminoethyl methanesulfonate hydrochloride from 2-dimethylaminoethanol and methanesulfonyl chloride has been reported,[3] and while our work was in progress the preparation of 1-dimethylamino-2-propyl methanesulfonate hydrochloride by a similar procedure was described.[4]

Monoalkylaminoalcohols (2-cyclohexylaminoethanol, 2-*n*-amylaminoethanol and 1-cyclohexylamino-2-propanol) were converted to the sulfonic acid ester hydrochlorides listed in Table I by first preparing their hydrochlorides to block amide formation, and then adding various aliphatic and aromatic sulfonyl chlorides in chloroform containing one to four equivalents of pyridine at 0° (Procedure A). The yields of esters obtained from the primary alcohols were much higher (29–67%) than from the secondary alcohol, 1-cyclohexylamino-2-propanol (16%). A side reaction which occurred at higher temperatures in the preparation of 2-cyclohexylaminoethyl methanesulfonate hydrochloride was a displacement of the methanesulfonate ester group by chloride, forming 2-cyclohexylaminoethyl chloride hydrochloride, in an alkylation which for convenience can be represented as

(1) Sharp and Dohme Research Associate.

(2) The patents concerned are listed by K. H. Slotta and R. Behnisch, *Ann.*, **497**, 170 (1932).

(3) R. D. Haworth, A. H. Lamberton and D. Woodcock, *J. Chem. Soc.*, 182 (1947).

(4) N. L. Wendler and M. Tishler, THIS JOURNAL, **71**, 374 (1949).

TABLE I: AMINOALKYL SULFONIC ACID ESTER HYDROCHLORIDES

Number	Ester hydrochloride	M.p., °C.[a]	Yield, %	Procedure	Time, hours	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
1	$CH_3SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl	141–141.6	67	A[e]	90	$C_9H_{20}NO_3SCl$	41.93	41.88	7.82	7.81	5.43	5.32
1	$CH_3SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl		32	B	1.8							
2	n-$C_4H_9SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl	115.6–116.8	52	A[f]	120	$C_{12}H_{26}NO_3SCl$	48.06	47.94	8.74	8.84	4.67	4.57
3	n-$C_6H_{13}SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl	116.4–117.4	61	A[f]	121	$C_{14}H_{30}NO_3SCl$	51.28	51.48	9.22	9.24	4.27	4.25
4	$C_6H_5CH_2SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl	118.2–119.6	57	A[f]	18	$C_{15}H_{24}NO_3SCl$	53.96	53.72	7.25	7.22	4.20	4.34
5	$C_6H_5SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl	111.2–112	29	A[f]	15[i]	$C_{14}H_{22}NO_3SCl$	52.57	52.51	6.93	7.01	4.38	4.26
6	p-$CH_3C_6H_4SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl[b]	133.4–134	40	A[f]	18[i]	$C_{15}H_{24}NO_3SCl$	53.96	53.82	7.25	7.26	4.20	4.07
7	p-$NO_2C_6H_4SO_2OCH_2CH_2NHC_6H_{11}$ (-cyclo)·HCl	103.6–104	51	A[f]	18[i]	$C_{14}H_{21}N_2O_5SCl$	46.08	46.05	5.80	5.70	7.68	7.66
8	$C_6H_5CH_2SO_2OCH_2CH_2NHC_6H_{11}$ (-n)·HCl	115–115.4	41	A[f]	18	$C_{14}H_{24}NO_3SCl$	52.24	52.07	7.52	7.53	4.35	4.28
9	$CH_3SO_2OCH_2CH_2N(CH_3)_2$·HCl[c,j]	99–102.4[g]	70	A[g]	48	$C_5H_{14}NO_3SCl$	29.48	29.51	6.93	6.88	6.88	6.59
9	$CH_3SO_2OCH_2CH_2N(CH_3)_2$·HCl[c,j]		74	C	2							
10	$CH_3SO_2OCH_2CH_2N(C_2H_5)_2$·HCl[d,k]	88.4–89.2	36	B	2.3	$C_7H_{18}NO_3SCl$	36.28	36.05	7.83	8.02	6.04	6.13
10	$CH_3SO_2OCH_2CH_2N(C_2H_5)_2$·HCl[d,k]		61	C	2							
11	$CH_3SO_2OCH(CH_3)CH_2NHC_6H_{11}$ (-cyclo)·HCl	115.4–116.8	16	A[h]	101	$C_{10}H_{22}NO_3SCl$	44.19	44.25	8.16	8.26	5.15	5.03
11	$CH_3SO_2OCH(CH_3)CH_2NHC_6H_{11}$ (-cyclo)·HCl		11	C	2							

[a] Samples in sealed melting point tubes were placed in a bath 5° below the melting point and the temperature was raised 2° per minute. [b] The picrate was prepared as a derivative from the hydrochloride and picric acid in hot ethanol and recrystallized from ethanol; m.p. 137.2–138°. *Anal.* Calcd. for $C_{21}H_{26}N_4O_{10}S$: C, 47.90; H, 4.98; N, 10.64. Found: C, 48.02; H, 5.02; N, 10.57. [c] The picrate, prepared and recrystallized as described in footnote *b*, melted at 122–123.2°. *Anal.* Calcd. for $C_{11}H_{16}N_4O_{10}S$: C, 33.33; H, 4.07; N, 14.14. Found: C, 33.38; H, 4.13; N, 14.39. [d] The picrate, prepared as described in footnote *b* and recrystallized from a mixture of ethyl acetate and ether, melted at 76.2–77.6°. *Anal.* Calcd. for $C_{13}H_{20}N_4O_{10}S$: C, 36.79; H, 4.75; N, 13.20. Found: C, 36.73; H, 4.78; N, 13.23. [e] Using 4 equivalents of pyridine. [f] Using 2 equivalents of pyridine. [g] Using the free base (2-dimethylaminoethanol) and omitting the pyridine. Dr. E. L. Engelhardt of Sharp and Dohme, Inc., has also obtained this compound in a higher melting (presumably dimorphous) form, m.p. 120–121°. [h] Using 1 equivalent of pyridine. [i] At a reaction temperature of 5 to 15°. [j] In ref. 3 the melting point of the monohydrate of this compound is reported as 97°. Our product was anhydrous but very hygroscopic. Neutral equivalent: calcd., 203.7; found, 206.4. [k] This hygroscopic salt was recrystallized from a mixture of absolute ethanol and acetone.

occurring through reaction with pyridine hydrochloride.[5]

$$CH_3SO_2OCH_2CH_2NHC_6H_{11}\cdot HCl + C_5H_5N\cdot HCl \longrightarrow C_6H_{11}NHCH_2CH_2Cl\cdot HCl + C_5H_5N\cdot CH_3SO_3OH$$

It was unnecessary to block the tertiary amino group of 2-dimethylaminoethanol by conversion to the hydrochloride prior to treatment with methanesulfonyl chloride, and these reactants at 0° yielded 70% of the ester hydrochloride (Table I). Methanesulfonyl chloride and 2-diethylaminoethanol failed to form the ester hydrochloride in good yield, however, probably because of an alkylation reaction which occurred exothermically when the mixture was not cooled, forming a tetraethylpiperazinium salt[6] that was isolated in 60% yield as the dichloride (I), and further characterized as the dipicrate.

Another method of esterification, through which it was possible to prepare diethylaminoethyl methanesulfonate hydrochloride, consisted in conversion of the aminoalcohols to the sodium alkoxides with sodium hydride in ether, followed by addition of the sulfonyl chloride at −10° (procedure B). After separating the sodium chloride formed, the hydrochlorides were prepared by introducing dry hydrogen chloride into the cold ether solutions. Better yields of the esters were obtained by a modification of this method in which an inverse order of addition was used (the sodium alkoxide was added to the sul-

$$2CH_3SO_2Cl + 2HOCH_2CH_2N(C_2H_5)_2 \longrightarrow 2CH_3SO_2OCH_2CH_2N(C_2H_5)_2\cdot HCl \longrightarrow$$

I

[5] The reaction of alkyl *p*-toluenesulfonates with pyridine hydrochloride forming alkyl chlorides has been reported by K. Hess and H. Stenzel, *Ber.*, **68**, 981 (1935).

[6] Under more favorable conditions for piperazine formation, K. H. Slotta and R. Behnisch (ref. 2) have reported preparation of a number of piperazinium salts from β-aminoalcohols and sulfonyl chlorides.

fonyl chloride, Procedure C). About 10% yields of N-methanesulfonyl 2-cyclohexylaminoethyl methanesulfonate (II) and N-methanesulfonyl-1-cyclohexylamino-2-propyl methanesulfonate (III) (amide esters formed by reaction at both the amino nitrogen and hydroxyl groups) were formed as by-products from 2-cyclohexylaminoethanol by procedure B and 1-cyclohexylamino-2-propanol by procedure C.

$$CH_3SO_2OCH_2CH_2N(C_6H_{11})SO_2CH_3$$
II

$$CH_3SO_2OCH(CH_3)CH_2N(C_6H_{11})SO_2CH_3$$
III

A molecular rearrangement by a displacement reaction was observed to occur when 2-cyclohexylaminoethyl *p*-toluenesulfonate hydrochloride was heated slightly above its melting point for a few minutes; the isomeric *p*-toluenesulfonic acid salt of 2-cyclohexylaminoethyl chloride was formed in high yield.

$$p\text{-}CH_3C_6H_4SO_2OCH_2CH_2NHC_6H_{11}\cdot HCl \longrightarrow$$
IV
$$C_6H_{11}NHCH_2CH_2Cl\cdot p\text{-}CH_3C_6H_4SO_2OH$$
V

A similar rearrangement in which 1-dimethylamino-2-propyl methanesulfonate hydrochloride formed 1-dimethylamino-2-chloropropane on heating has been reported by Wendler and Tishler.[4]

Pharmacological

We are indebted to Dr. Karl H. Beyer, Robert T. Ford and Samuel E. McKinney of Sharp and Dohme, Inc., for preliminary pharmacological studies of the aminoalkyl sulfonic acid ester hydrochlorides listed in Table I (identified hereafter by the numbers in column 1 of Table I). Numbers 1–7, 9 and 10 were tested for local anesthetic activity in the rabbit's cornea at 1% concentration. Anesthesia of about two minutes duration was produced by no. 1 and 2, and of 10 minutes duration by no. 3; the remainder were inactive. Compounds 1–10 administered intravenously to dogs (2 mg./kg.) produced a decrease in blood pressure of one to two minutes duration and 10–20% magnitude for no. 3, 7 and 8, and less than 10% for the others. The effect on the heart rate was small in all cases; no. 9 produced a marked increase (66–116%) in respiratory rate. Samples 1–10 showed no significant degree of protection against 1:1,000,000 histamine (Guinea pig intestinal strip method) at dilutions greater than 1:10,000, but no. 3, 4, 5, 6 and 8 gave essentially complete protection at 1:10,000 dilution. None of the samples (1–10) showed significant analgesic activity (rat tail method) at doses of one-tenth the LD_{50}. The following acute toxicities in mg./kg. were observed on intravenous injection of 0.25–1.0% solutions into female Carworth Farms mice: 1, 267 ± 35; 2, 75 ± 10; 3, 35 ± 5; 4, 52 ± 5; 5, 53 ± 7; 6, 72 ± 5; 7, 140 ± 19; 8, 93 ± 7; 9, 55 ± 7; 10, 86 ± 10 (all in terms of the free esters, calculated from the weights of the hydrochlorides which were injected; ten mice were used at each dose level).

Experimental[7]

Aminoalcohols and Sulfonyl Chlorides.—2-Cyclohexylaminoethanol, 2-*n*-amylaminoethanol and 1-cyclohexylamino-2-propanol were prepared by catalytic reductive alkylation of the primary aminoalcohols,[8] and converted to hydrochlorides by treatment with dry gaseous hydrogen chloride in ether. 2-Dimethylaminoethanol and 2-diethylaminoethanol were redistilled commercial products (Carbide and Carbon Chemicals Corp.). The sulfonyl chlorides were purified commercial products, except for *n*-butanesulfonyl chloride, phenylmethanesulfonyl chloride and *n*-hexanesulfonyl chloride, which were prepared by chlorinating the crude dialkyl disulfides, prepared in the first two cases from the Bunte salts and in the last from the isothiuronium salt.[9]

Aminoalkyl Sulfonic Acid Ester Hydrochlorides (Table I). Procedure A.—The preparation of 2-cyclohexylaminoethyl methanesulfonate hydrochloride illustrates procedure A. 2-Cyclohexylaminoethanol hydrochloride (3.6 g., 0.20 mole) and pyridine (6.3 g., 0.08 mole) were dissolved in 20 ml. of reagent grade chloroform. The solution was stirred and cooled in an ice–salt-bath, and methanesulfonyl chloride (2.9 g., 0.025 mole) was added dropwise while the reaction temperature was maintained at −1 to +2°. The mixture was allowed to stand at 2° in a refrigerator for 90 hours, and the solid product was separated by filtration, washed with dry ether, and recrystallized to constant melting point from absolute ethanol. When the product was soluble in chloroform, as in the case of 2-cyclohexylaminoethyl *n*-hexanesulfonate hydrochloride, the solvent was removed under reduced pressure, with warming in a water-bath that was not allowed to rise above 50°, and the viscous residue was washed with dry ether before crystallization. All of the esters prepared by this procedure (Table I) were recrystallized from absolute ethanol, except 2-cyclohexylaminoethyl *p*-nitrobenzenesulfonate hydrochloride, which was crystallized by adding ether to a solution in a large volume of ethanol at room temperature to the point of cloudiness and cooling to −15°, in order to avoid formation of a by-product (probably by rearrangement as in the conversion of IV to V).

One side reaction which occurred at higher temperatures was observed in the reaction of methanesulfonyl chloride with 2-cyclohexylaminoethanol hydrochloride in chloroform-containing pyridine (1 equivalent). The temperature increased from 0° to the boiling point during the exothermic reaction, and one product that was isolated by crystallization from ethanol was 2-cyclohexylaminoethyl chloride hydrochloride, m.p. and mixed m.p. with an authentic sample,[10] 217.6–218.4°.

Procedure B.—The preparation of 2-diethylaminoethyl methanesulfonate hydrochloride (Table I) provides an example of procedure B. Sodium hydride (1.0 g., 0.042 mole) was added to 75 ml. of dry ether in a 200-ml. three-necked flask fitted with a sealed stirrer, a dropping funnel and a reflux condenser, and protected from atmospheric moisture with drying tubes. 2-Diethylaminoethanol (4.8 g., 0.041 mole) was added over a period of 20 minutes with stirring, which was continued for 2 hours, while hydrogen was evolved and the sodium alkoxide formed. The condenser was replaced by a thermometer, and methanesulfonyl chloride (4.7 g., 0.041 mole) was added dropwise with stirring over a period of 30 minutes at a reaction temperature of −10 to −6° maintained by a bath of Dry Ice and trichloroethylene. Dry ether (25 ml.) was added so that the mixture could be stirred more efficiently, and stirring was continued for 2 hours at −10 to −14°. The mixture was filtered rapidly with suction into a flask cooled with Dry Ice, and the solid on the funnel was washed with several portions of dry ether. Dry hydrogen chloride was passed through the filtrate to precipitate the product as the hydrochloride, which was washed with dry ether and recrystallized from a mixture of dry ethanol and ether (properties in Table I).

(7) Melting points are corrected. We are indebted to Mr. S. M. Nagy and his associates for analyses.

(8) A. C. Cope and E. M. Hancock, THIS JOURNAL, **64**, 1503 (1942); *ibid.*, **66**, 1453 (1944).

(9) C. Ziegler and J. M. Sprague, *J. Org. Chem.*, **16**, 621 (1951).

(10) A. C. Cope, H. R. Nace, W. R. Hatchard, W. H. Jones, M. A. Stahmann and R. B. Turner, THIS JOURNAL, **71**, 554 (1949).

In the preparation of 2-cyclohexylaminoethyl methanesulfonate hydrochloride by this procedure about 10% of N-methanesulfonyl-2-cyclohexylaminoethyl methanesulfonate (II) was isolated by adding the ether-insoluble material to cold water, separating the solid that was insoluble in water, and recrystallizing from ethanol; m.p. 76–77.6°. This product was identical (mixed melting point) with an authentic sample of II prepared in 24% yield from 2-cyclohexylaminoethanol, methanesulfonyl chloride and aqueous sodium hydroxide by a Schotten–Baumann procedure and recrystallized from ethanol; m.p. 77.2–77.6°.

Anal. Calcd. for $C_{10}H_{21}NO_5S_2$: C, 40.12; H, 7.07. Found: C, 40.16; H, 7.04.

Procedure C.—The following preparation of 2-dimethylaminoethyl methanesulfonate hydrochloride illustrates procedure C. The sodium alkoxide was prepared from 7.3 g. (0.082 mole) of 2-dimethylaminoethanol and sodium hydride (3.0 g., 0.123 mole) in 150 ml. of dry ether as in procedure B, with refluxing for four hours to complete the reaction. A solution of methanesulfonyl chloride (9.4 g., 0.082 mole) in 150 ml. of dry ether was placed in a 500-ml. three-necked flask fitted with a sealed stirrer, a dropping funnel and a thermometer extending into the liquid. The solution was cooled to −8° with Dry Ice and trichloroethylene, and the suspension of the sodium alkoxide was added dropwise over a period of 40 minutes at −8 to −5°. Precipitation of sodium chloride occurred immediately, and the mixture was stirred at −8 to −5° for one hour after the addition was completed. The product (Table I) was isolated as the hydrochloride in the manner described under procedure B.

About 10% of N-methanesulfonyl-1-cyclohexylamino-2-propyl methanesulfonate (III) was isolated as a by-product in the preparation of 1-cyclohexylamino-2-propyl methanesulfonate hydrochloride by this procedure. The ether-insoluble solid was combined with material obtained by concentrating the ethereal filtrate from the ester hydrochloride, washed with water, and recrystallized from methanol to a constant melting point of 100.8–101.8°.

Anal. Calcd. for $C_{11}H_{23}NO_5S_2$: C, 42.15; H, 7.40; N, 4.47. Found: C, 42.14; H, 7.35; N, 4.50.

Tetraethylpiperazinium Dichloride (I).—A solution of 2.6 g. of methanesulfonyl chloride in 5 ml. of dry ether was added to 2.0 g. of 2-diethylaminoethanol without cooling, producing an exothermic reaction that raised the temperature to a maximum of 82°. The resulting oil was dissolved in absolute ethanol, and the solution was saturated with dry hydrogen chloride, with cooling in ice. Addition of dry ether precipitated tetraethylpiperazinium dichloride (I); 1.4 g. (60%), m.p. 274–275° (dec.) (ref. 2 reports m.p. 277°). The dichloride was characterized by conversion to the dipicrate, which after recrystallization from aqueous ethanol melted at 267° (dec.). Since ref. 2 reports m.p. 277° for the dipicrate, an authentic sample of the dipicrate (identical according to mixed melting point with the sample derived from I) was prepared from tetraethylpiperazinium di-*p*-toluenesulfonate[2]; m.p. 268° (dec.).

Anal. Calcd. for $C_{24}H_{32}N_8O_{14}$: C, 43.90; H, 4.91; N, 17.07. Found: C, 44.03; H, 5.11; N, 17.16.

Rearrangement of 2-Cyclohexylaminoethyl *p*-Toluenesulfonate Hydrochloride (IV) to the *p*-Toluenesulfonic Acid Salt of 2-Cyclohexylaminoethyl Chloride (V).—2-Cyclohexylaminoethyl *p*-toluenesulfonate hydrochloride (IV) (2.0 g.) was melted by heating in a bath at 130–150° for 10 minutes. On cooling, the melt solidified; 1.7 g., m.p. 147–150°. Three crystallizations from acetone yielded 1.4 g. of the isomeric *p*-toluenesulfonic acid salt of 2-cyclohexylaminoethyl chloride (V) with a constant melting point of 151–151.6°.

Anal. Calcd. for $C_{15}H_{24}NO_3SCl$: C, 53.96; H, 7.25; N, 4.20. Found: C, 53.93; H, 7.26; N, 4.36.

The rearrangement product V was soluble in water, and gave a negative test for chloride ion with aqueous silver nitrate. A solution of 0.92 g. of V in 20 ml. of water became turbid upon addition of a slight excess of sodium hydroxide, and extraction with ether followed by drying the extract over calcium chloride and introduction of dry hydrogen chloride precipitated 0.425 g. of 2-cyclohexylaminoethyl chloride hydrochloride, m.p. and mixed m.p. with a known sample,[10] 217.4–218.8°. The sodium *p*-toluenesulfonate present in the aqueous solution was identified by conversion into the *p*-toluenesulfonic acid salts of *p*-nitrobenzamidine and *p*-toluidine, which were identical in melting point and mixed melting point with authentic samples. The rearrangement product V also was characterized by direct comparison with an authentic sample (identical by melting point and mixed melting point) prepared from 2-cyclohexylaminoethyl chloride and *p*-toluenesulfonic acid.

CAMBRIDGE, MASSACHUSETTS RECEIVED AUGUST 8, 1951

[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Studies on Lignin and Related Products. VII.[1] The Isolation of Certain Compounds from Lignin Oxidation Mixtures by Chromatographic Techniques[2,3]

BY IRWIN A. PEARL AND EDGAR E. DICKEY

Because the complex nature of fractions obtained by oxidizing lignosulfonate materials with cupric oxide and alkali precluded their complete analysis by heretofore employed procedures, recourse was made to adsorption chromatography. By means of this technique, the sodium bisulfite-soluble and the alkali-soluble fractions from such oxidations have yielded, in addition to previously isolated compounds, the following new oxidation products: 4,4′-dihydroxy-3,3′-dimethoxychalcone, 4,4′-dihydroxy-3,3′-dimethoxybenzil, 4,4′-dihydroxy-3,3′-dimethoxybenzophenone, and an unidentified isomer of dehydrodivanillin which is probably a dihydroxydimethoxyformylbenzophenone. Although the isolation of these products can be explained by assuming their resynthesis from vanillin or the like originally formed by degradation of the lignin, there is also a possibility that some of the C_6–C_3 units in the lignin structure are linked together through the α-carbon atoms.

In a recent communication[4] the isolation and identification of vanillin, guaiacol, acetovanillone, vanillic acid, 5-carboxyvanillin (I), 5-carboxyvanillic acid (II), dehydrodivanillin (III) and dehydrodivanillic acid (IV) from alkaline cupric oxide oxidations of fermented (*Torulopsis utilis*) spent sulfite liquor was reported. These isolations were effected by chemical separations and fractionations by means of solubility differences in various solvents and solvent combinations. During the above work it became obvious that the complex nature of the various fractions precluded their complete analysis by these two methods alone. Recourse was made to adsorption chromatography, a technique which recently was demonstrated to give exceptionally good results in the

(1) For paper VI of this series, see *Tappi*, **33**, 544 (1950).

(2) Presented before the Division on Pulp Cell-Wall Constituents at the XIIth International Congress of Pure and Applied Chemistry, New York, N. Y., September 10–13, 1951.

(3) This paper represents a portion of the results obtained in the research program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

(4) I. A. Pearl, THIS JOURNAL, **72**, 2309 (1950).