Anal. Calcd. for $C_4H_{11}NCl_2$: C, 33.35; H, 7.70; N, 9.72. Found: C, 33.57; H, 7.74; N, 9.92.

By treatment of 1-amino-2-methyl-2-propanol with 12 *N* hydrochloric acid at the boiling point for one hour no 2-chloro-1-amino-2-methylpropane was formed.

2-Chloro-1-amino-2-methylpropane Picrate.—The picrate of 2-chloro-1-amino-2-methylpropane was prepared in 79% yield by neutralizing a solution of the corresponding hydrochloride with sodium picrate solution; m.p. 166–167°. One recrystallization from water gave an analytical sample, m.p. 169.0–170.0°. Dersin[12a] reported the m.p. 159° and gave no analysis.

Anal. Calcd. for $C_{10}H_{13}N_4O_7Cl$: C, 35.67; H, 3.89; N, 16.64. Found: C, 35.82; H, 4.01; N, 16.35.

1-Chloro-2-amino-2-methylpropane Picrate.—The picrate of 1-chloro-2-amino-2-methylpropane was prepared in 78% yield in like manner. Two recrystallizations from water gave an analytical sample, m.p. 177.0–178.0°. A lower melting point was obtained by recrystallization from ethanol.

Anal. Calcd. for $C_{10}H_{13}N_4O_7Cl$: C, 35.67; H, 3.89; N, 16.64. Found: C, 35.81; H, 4.00; N, 16.77.

Determination of Rate Constants.—The rates of formation of 1-chloro-2-amino-2-methylpropane (II) and 1-amino-2-methyl-2-propanol given in Table I were determined on the assumption that the formation of these two compounds was the only reaction consuming 2,2-dimethylethylenimine in its hydrolysis with 1 *N* hydrochloric acid. The percentage of chloroamine II was determined accurately by titration with sodium hydroxide to a methyl orange end-point (within 1%) and the remainder was presumed to be amino alcohol IV. The validity of the analytical method was tested on the two pure chloroamines II and III. When either of these hydrochlorides was dissolved in hydrochloric acid the excess acid was accurately measured by the end-point of methyl orange with sodium hydroxide solution.

From the product ratio and the per cent. chloroamine formed at each point, the total rate of disappearance of 2,2-dimethylethylenimine was determined for each reaction. The validity of the method was demonstrated by plotting, as for a single first-order reaction, the logarithm of the per cent. imine remaining in solution against time. These data gave straight lines for the reactions run at 35° or lower and only a slight curvature for the reaction at 62°.

The first-order rate constant for the total reaction is given by

$$k_T = \frac{2.303}{t} \log \frac{C_0}{C} = \frac{2.303}{t} \log \frac{100}{P}$$

where C_0 is initial concentration of imine and C is concentration at the time t, for which P, per cent. imine remaining at time t, may be substituted. The rate constant, k_T, then is the slope of the line obtained by plotting log P against t. If now the per cent. yield of each product is a measure of its rate contribution, then $k_T = k_{Cl} + k_{alc}$.

Activation energies for the two reactions were calculated by the method of least squares from the rate constants at four temperatures in 1 *N* acid.

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[CONTRIBUTION FROM THE METCALF LABORATORIES, BROWN UNIVERSITY]

Reactions of Ethylenimines. VI. Picrates

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The picrate of 2,2-dimethylethylenimine (I) rearranges upon heating in inert solvents into the picramide (IV) of 1-amino-2-methyl-2-propanol. Alcohols and phenol acting on the ethylenimine picrates open the imine ring at the more substituted carbon to give β-amino ethers, of the type $R_1R_2(R_3O)CCH_2NH_2$. The aliphatic β-aminoethers may be recovered from the corresponding picrates in 54–83% yields.

The ethylenimine ring has been found to open in the presence of weak acids such as thiophenol,[2] phenols[3] and benzoic acids[4] but forms a stable picrate[5] in non-protonic solvents.

In attempting to purify the picrate of 2,2-dimethylethylenimine by recrystallization from various solvents it was found that the product melted at a constant point (124–126°) but the melt was always opaque until a temperature of 160° was reached. Further investigation revealed that the picrate I rearranged on heating to the picramide of 1-amino-2-methyl-2-propanol (IV) (m.p. 160°). In polar solvents such as acetonitrile and nitromethane, the 2,2-dimethylethylenimmonium picrate (I) rearranged to the extent of 40% and only slightly less in ethyl acetate or methyl ethyl ketone. The picramide IV was identified by direct synthesis from 1-amino-2-methyl-2-propanol and picryl chloride.

No new theory seems necessary to account for this rearrangement. Isolation of ether picrates of type V suggests the ether II as a logical intermediate in the present case. Migrations from O to N by acyl groups through a heterocyclic five-membered ring are well established in the literature.[6] By analogy, the picryl group which resembles an acyl group in many ways could participate in the five-membered heterocyclic intermediate III in the path to the picramide IV.

Alternatively, the rearrangement may be considered as one of the Smiles[7] type as exemplified in the work of Roberts.[8] However, only amino diaryl ethers have been reported to take part in Smiles rearrangements.

When the picrate of 2,2-dimethylethylenimine was refluxed in a reacting solvent such as methanol or ethanol, ring opening by the alcohol[9] predominated over the rearrangement and amino ether picrates of type V were formed (Table I). No appreciable ring opening took place with *n*-propyl or isopropyl alcohols as solvents and the imine picrate was recovered unchanged in short heating periods. Upon prolonged heating in these solvents some re-

(1) (a) Taken in part from Senior theses for the Sc.B. degree, Brown University; (b) Edwin P. Anthony Fellow, 1952–1954.

(2) G. Meguerian and L. B. Clapp, THIS JOURNAL, **73**, 2121 (1951).

(3) L. B. Clapp, *ibid.*, **73**, 2584 (1951).

(4) D. H. Powers and V. B. Schatz, unpublished data, Brown University.

(5) V. B. Schatz and L. B. Clapp, THIS JOURNAL, **77**, 5113 (1955).

(6) See for example: E. E. van Tamelen, THIS JOURNAL, **73**, 5773 (1951); G. Fodor and J. Kiss, *ibid.*, **72**, 3495 (1950); *Acta Chim. Hung.*, **1**, 130 (1951); *J. Chem. Soc.*, 1589 (1952).

(7) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 362 (1951).

(8) K. C. Roberts and C. G. De Worms, *J. Chem. Soc.*, 727 (1934); K. C. Roberts, C. G. De Worms and H. B. Clark, *ibid.*, 196 (1935).

(9) D. S. Tarbell and D. K. Fukushima, THIS JOURNAL, **68**, 2499 (1946).

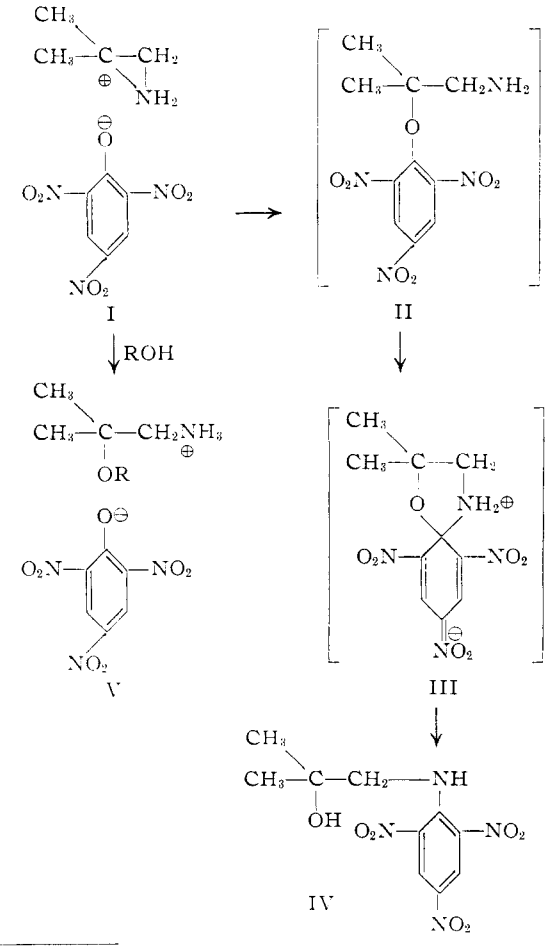
TABLE I

PICRATES OF ETHYLENIMINES AND AMINO ETHERS

R_1	R_2	R_3	M.p., °C.	Yield, %	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
Ethylenimines, $R_1R_2C(-NH-)CH_2$										
H	H		125–127[a]	96	35.30	2.96	20.59	35.68	3.00	20.45
CH_3	CH_3		124–126[b]	99						
C_2H_5	H		103–104	97	40.01	4.03	18.65	40.13	4.28	18.57
Amino ethers, $R_1R_2(R_3O)C-CH_2NH_2$										
H	H	C_2H_5	121–123[c]	88						
H	H	CH_3	149.2–150.4	91	35.53	3.98	18.42	36.09	4.20	18.29
C_2H_5	H	C_2H_5	158–159[d]	86						
C_2H_5	H	CH_3	148.0–150.6	80	39.76	4.86	16.86	39.98	5.16	16.61
CH_3	CH_3	CH_3	177.0–178.5	83	39.76	4.86	16.86	39.90	4.90	16.84
CH_3	CH_3	C_6H_5	200.0–200.5[e]	20	48.73	4.60	14.21	48.60	4.71	13.83

[a] M.p. 142° was reported by S. Gabriel, *Ber.*, **21**, 1049 (1888). [b] Reference 5. [c] L. Knorr and G. Meyer, *Ber.*, **38**, 3130 (1905). [d] M.p. 156° was reported, reference 11a, and 152–154°, reference 11c. [e] The phenylthiourea of this amino ether had a m.p. 113.0–114.0°. *Anal.* Calcd. for $C_{17}H_{20}N_2OS$: C, 67.96; H, 6.71; N, 9.33. Found: C, 67.77; H, 6.82; N, 8.98.

arrangement to IV occurred. Tarbell[10] had established the point of ring opening of the imine picrate with an alcohol as the more substituted carbon. This was verified in the present work in the following case. The picrate of 2-ethylethylenimine opened with ethanol to give β-ethoxybutylamine, whose structure was known from an independent synthesis.[11] It is also known[5] that water opens the ring in 2,2-dimethylethylenimmonium picrate at the tertiary carbon.



Warming the same picrate with phenol also opened the ring (probably at the same point) of the imine to give the ether V where R is phenyl. The yield was low (20%) and the reaction was accompanied by deammonation to form picramide (50%) and ammonium picrate (13%). The structure of the phenyl ether was not proved by an independent synthesis but the isomeric β-aminoisobutyl phenyl ether[3] whose structure is known was excluded by comparison of derivatives.

The amino ethers (Table II) were recovered from the picrates in fair yields (54–83%) and this may prove a useful path to the synthesis of some physiologically interesting compounds.[12]

TABLE II

PHYSICAL CONSTANTS OF AMINO ETHERS, $R_1R_2(R_3O)C-CH_2NH_2$

R_1	R_2	R_3	B.p., °C.	Yield, %	$n^{25}D$	d^{25}_4	M_D Calcd.	M_D Found
H	H	C_2H_5	105–108[a]	83				
H	H	CH_3	92–96[b]	54				
C_2H_5	H	C_2H_5	138–141[c]	56				
C_2H_5	H	CH_3	118–121[d]	67	1.4112	0.8431	30.36	30.39
CH_3	CH_3	CH_3	117–119[e]	68	1.4173	.8606	30.36	30.17

[a] L. Knorr, *Ber.*, **37**, 3506 (1904). [b] W. Traube and E. Peiser, *ibid.*, **53**, 1507 (1920). [c] Reference 11a. [d] *Anal.* Calcd. for $C_5H_{13}NO$: C, 58.21; H, 12.70; N, 13.58. Found: C, 57.99; H, 12.78; N, 13.44. [e] *Anal.* Calcd. for $C_5H_{13}NO$: C, 58.21; H, 12.70; N, 13.58. Found: C, 58.28; H, 12.34; N, 13.50.

Experimental[13]

Ethylenimmonium Picrates.—The three imine picrates described in Table I were prepared by the method pre-

(10) D. S. Tarbell and P. Noble, Jr., THIS JOURNAL, **72**, 2657 (1950).

(11) (a) S. Bookman, *Ber.*, **28**, 3111 (1895); (b) M. de Montmollin and E. Zolliker, *Helv. Chim. Acta*, **12**, 611 (1929); (c) M. de Montmollin and F. Achermann, *ibid.*, **12**, 876 (1929).

(12) Compare C. D. Hurd and P. Perletz, THIS JOURNAL, **68**, 38 (1946).

(13) Melting points given to tenths of a degree are corrected. Boiling points are not corrected. Analyses by S. M. Nagy, Microchemical Laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts.

viously published.[5] The melting points of none of the three were raised by attempted recrystallization.

Picramide of 1-Amino-2-methyl-2-propanol (IV).—Four and two-tenths grams (0.014 mole) of 2,2-dimethylethylenimmonium picrate was refluxed for one hour in 15 ml. of acetonitrile. Most of the acetonitrile was then removed by passing dry air over the reaction mixture. Ethyl acetate (3 ml.) was added and the mixture was cooled in ice. The yellow picramide of 1-amino-2-methyl-2-propanol was removed by filtration and washed once with 2 ml. of ice-cold ethyl acetate; yield 1.65 g. (40%), m.p. 156–158°. Sublimation at 140° (0.4 mm.) gave an analytical sample, m.p. 160.6–161.6°.

The structure of the picramide was established by an independent synthesis. Equivalent amounts of picryl chloride and 1-amino-2-methyl-2-propanol were allowed to react in absolute ethanol. This picramide had a m.p. 158–160° and a mixed m.p. with the preparation just described was not depressed.

Anal. Calcd. for $C_{10}H_{12}N_4O_7$: C, 40.01; H, 4.03; N, 18.65. Found: C, 40.16; H, 4.22; N, 18.33.

β-Aminoether Picrates (V). A. β-Methoxybutylammonium Picrate.—The following preparation is a representative procedure used in making the aliphatic aminoether picrates described in Table I.

B. **β-Phenoxyisobutylammonium Picrate.**—2,2-Dimethylethylenimmonium picrate (21 g., 0.07 mole) was kept at 80° with 20 g. of phenol (0.21 mole) for 2 hours and then was allowed to stand overnight. The reaction mixture was filtered without cooling to remove 2.27 g. (13%) of ammonium picrate.

Ethanol (40 ml. of 95%) was added to the filtrate and upon cooling 8 g. of a brown, crystalline precipitate was obtained. Two successive additions of 20 ml. of 50% ethanol gave a total yield of 13.9 g. of crude material, m.p. 150–165°. The crude product was extracted with 95% ethanol to give 5.65 g. (20%) of β-phenoxyisobutylammonium picrate, m.p. 195–200°. Repeated recrystallization from absolute ethanol gave an analytical sample, m.p. 200.0–200.5°. Analytical data appear in Table I.

The residue from the ethanol extraction was determined to be picramide in a mixed m.p. with an authentic sample, m.p. 188–190°; yield 8.0 g. (50%).

β-Phenoxy-*t*-butylammonium Picrate.—One-half gram (0.003 mole) of β-phenoxy-*t*-butylamine[3] in 5 ml. of toluene was added dropwise to 0.70 g. (0.003 mole) of picric acid dissolved in 10 ml. of toluene. The picrate (1.1 g., 91%) was washed with carbon tetrachloride and dried, m.p. 189–190°. Recrystallization from absolute ethanol gave an analytical sample, m.p. 194.0–195.0°

A mixture of this sample with that of β-phenoxyisobutylammonium picrate gave a lowered m.p. 175–190°. Since the structure of β-phenoxy-*t*-butylammonium picrate has been established[3] it is suggested that the picrate of m.p. 200.0–200.5° is the isomeric β-phenoxyisobutylammonium picrate. Therefore, 2,2-dimethylethylenimmonium picrate must have opened at the tertiary carbon with phenol as it does with alcohols.

Anal. Calcd. for $C_{16}H_{18}N_4O_8$: C, 48.73; H, 4.60; N, 14.21. Found: C, 48.76; H, 4.60; N, 14.15.

β-Aminoethers. β-Methoxybutylamine.—The amino ethers compiled in Table II were prepared by a method similar to the following procedure for β-methoxybutylamine.

The picrate of β-methoxybutylamine, m.p. 145–148° (33.2 g., 0.1 mole) was dissolved in 100 ml. of water, 150 ml. of concentrated hydrochloric acid was added, and the mixture was allowed to stand for 3 hours with occasional stirring. Picric acid was removed by filtration of the cold mixture and last traces were removed by extraction with 20-ml. portions of toluene until a last portion of toluene remained colorless. The water solution was evaporated nearly to dryness at room temperature and the aminoether hydrochloride was finally dried in a vacuum desiccator; yield 13 g. (93%). The amino ether hydrochloride was covered with 10 ml. of absolute methanol and treated with 6 g. (0.11 mole) of sodium methoxide. The reaction mixture was warmed one-half hour on the steam-bath, cooled, and filtered. Distillation removed the methanol and after a small forerun at 110–118°, the main fraction of β-methoxybutylamine was collected at 118–121°; yield 6.8 g. (67%).

The analysis for nitrogen on the aminoether prepared in this way resulted in a high value, evidently due to the presence of some ammonia in the sample. The aminoether was therefore converted to the hydrochloride in ether solution with dry hydrogen chloride. The hydrochloride was recrystallized from acetone to remove ammonium chloride but was so hygroscopic the melting point could not be determined. The solid hydrochloride was allowed to stand on solid potassium hydroxide which had been covered with anhydrous ether. After adding a trace of water and allowing to stand a week, the ether solution of the amino ether was fractionated to give pure β-methoxybutylamine, b.p. 118–121°, of constant refractive index. Physical constants and analyses appear in Table II.

PROVIDENCE 12, R. I.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY]

A New Aldehyde Synthesis and its Use in the Characterization of Organic Halides

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Aliphatic and aromatic Grignard reagents have been found to add to the double bond of the methiodide of 6-methyl-3-*p*-tolyl-3,4-dihydroquinazoline (II), itself formed by the reaction between *p*-toluidine, formaldehyde and formic acid. The resulting substituted tetrahydroquinazolines were hydrolyzed and the aldehydes of one more carbon atom converted directly to their 2,4-dinitrophenylhydrazone derivatives. A route to labeled aldehydes from labeled formaldehyde is suggested.

The conversion of a Grignard reagent to an aldehyde or aldehyde acetal with one more carbon atom has been accomplished by a great variety of reagents. The methods generally involve addition of a Grignard reagent to a C=X linkage (X = O,S,N) or the displacement of an alkoxide group from an orthoformate. Smith and Nichols,[2] after reviewing the field, conclude that N-ethoxymethyleneaniline and ethyl orthoformate are the most satisfactory reagents. The main disadvantage of ethyl orthoformate is the frequent necessity for the application of heat over long periods to cause the reaction to proceed at a reasonable rate while N-ethoxymethyleneaniline is costly and troublesome to prepare.

A new procedure, illustrated by the following reaction sequence I to V[3] accomplishes the same end without the above complications and further supplies the aldehyde as an easily hydrolyzed derivative III which may be converted directly to the corresponding 2,4-dinitrophenylhydrazone (IV). In spite of its apparent complexity the dihydroquina-

(1) Laboratory of Chemistry of Natural Products, National Heart Institute, National Institutes of Health, Department of Health, Education and Welfare, Bethesda 14, Maryland.

(2) L. I. Smith and J. Nichols, *J. Org. Chem.*, **6**, 489 (1941).

(3) This reaction sequence was evolved during a study of methods for the synthesis of di- and tetrahydroquinazolines in connection with U. S. Army Ordnance Project #DA-30-069-ORD-884.