analyzed for piperidinium chloride in the following manner: A 5.00-g. aliquot of the salts was treated with excess silver nitrate. The mixture of silver salts formed was acidified with nitric acid in ethanol to dissolve the coprecipitated silver 1,1-dinitroethane. The silver chloride left, upon being filtered and dried, weighed 1.14 g. The silver chloride isolated is equivalent to 1.40 g. of piperidinium chloride in the original precipitate of salts.

Filtrate I was concentrated at reduced pressure; a residue remained which contained crystals and weighed 21.2 g. The residue was extracted with a mixture of water and ether; the aqueous extract, upon ultraviolet analysis of an aliquot portion, was found to contain 5.01 g. of piperidinium 1,1-dinitroethane. The aqueous extract (an aliquot) upon treatment with silver nitrate (as described previously) yielded silver chloride equivalent to 0.81 g. of piperidinium chloride. The ether extract of the residue, after removal of the solvent, was vacuum-distilled to yield 1-chloro-1,1-dinitroethane (1.0 g.), b.p. 58–61° (22 mm.). The distillates: fractions 2 (1.92 g., b.p. 72–85° (3 mm.), $n^{20}\mathrm{D}$ 1.4840) and 3 (2.98 g., b.p. 85–88° (3 mm.), $n^{20}\mathrm{D}$ 1.4891) and a residue (3.0 g.) were not identified further.

The yield of products of reaction of 1-chloro-1,1-dinitroethane and piperidine were: piperidinium 1,1-dinitroethane (9.28 g., 48.3%), piperidinium chloride (2.21 g., 21.2%) and 1-chloro-1,1-dinitroethane (1.0 g., 6.5% recovery); the material balance was 62.8%.

1-Bromo-1,1-dinitroethane and Sodium Diethyl Malonate.—(a) 1-Bromo-1,1-dinitroethane (19.9 g., 0.10 mole) was added dropwise in 1 hr. to a stirred solution of sodium diethyl malonate (36.6 g., 0.20 mole) in absolute ethanol (220 ml.) at 5–10°. A yellow precipitate formed almost immediately after addition. The mixture was stirred at 25° for 20 hr. and then poured into anhydrous ether (400 ml.). The salts (21.3 g., ppt. 1) that precipitated were filtered, washed with ether and dried. The filtrate was evaporated nearly to dryness. Upon addition of anhydrous ether (300 ml.) a second solid (3.7 g., ppt. 2) separated. The filtrate was evaporated to one-fifth its volume and diluted with Skellysolve F. A pale-yellow solid (ppt. 3) precipitated, was filtered, washed with 1:5 ether–Skellysolve F and dried. Precipitate 3 was identified as **tetraethyl ethane-1,1,2,2-tetracarboxylate** (19.8 g., 62.3% yield), m.p. 74.5–76° (recrystallized from absolute ethanol). An authentic sample of tetraethylethane-1,1,2,2-tetracarboxylate[44] melted at 74.5–75.5°; the melting point was not depressed when the two samples were mixed.

The filtrate (from ppt. 3) was freed of solvents under vacuum to leave a residue weighing 10.8 g. An aliquot of this residue was diluted to a concentration of 0.0158 g./l. in 10^{-3} *M* aqueous sodium hydroxide; ultraviolet analysis of this solution showed that the residue contained 1.88 g. (15.7% yield) of **1,1-dinitroethane.** A 5.00-g. aliquot of the residue was vacuum distilled; the distillate, b.p. 59–68° (5 mm.), weighed 1.75 g. and was identified as a mixture of diethyl malonate and 1,1-dinitroethane (infrared spectrum). The distillation residue, on treatment with absolute ethanol (2 ml.) and Skellysolve F (5 ml.) gave **tetraethyl ethylenetetracarboxylate**[44] (1.06 g., 3.4% yield), m.p. 46–48°. The non-crystallizable part of the distillation residue weighed 2.04 g., $n^{20}\mathrm{D}$ 1.4402; the infrared spectrum of this material showed the presence of an ester group.

Aqueous silver nitrate (17 g. in 50 ml. of water) was added to a 10.00-g. aliquot of ppt. 1 in water (130 ml.). The silver salts (13.8 g.) that were obtained were filtered and washed with water. The salts were suspended in 50% aqueous ethanol (100 ml.), and 5 *N* nitric acid (50 ml.) was added to dissolve the coprecipitated silver 1,1-dinitroethane. The remaining silver bromide was filtered, washed with water, ethanol and ether and dried; wt. 7.83 g. This corresponds to 9.14 g. of **sodium bromide** in ppt. 1. Analysis of a sample of ppt. 1 by ultraviolet methods showed that its sodium 1,1-dinitroethane content was 8.52 g. The mixed salts in ppt. 2 were analyzed in the same manner as described for ppt. 1. The weight of **sodium bromide** was 1.21 g.; the weight of **sodium 1,1-dinitroethane** was 1.15 g. Impure tetraethyl ethane-1,1,2,2-tetracarboxylate (0.15 g.) was also isolated, m.p. 67–68°.

The reaction of 1-bromo-1,1-dinitroethane and sodium diethyl malonate is summarized: the yield of sodium 1,1-dinitroethane was 68%, 1,1-dinitroethane (15.7%), tetraethyl ethane-1,1,2,2-tetracarboxylate (63%), tetraethyl ethylenetetracarboxylate (3.4%) and sodium bromide (100%).

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[44] A. Kotz and G. Stalmann, *J. prakt. Chem.*, [2] **68**, 156 (1903); C. A. Bischoff and C. Rach, *Ber.*, **17**, 2781 (1884).

COLUMBUS 10, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Thiazolidine Chemistry. III. The Preparation and Reduction of Some 2-Phenyl-3-*n*-alkyl-4-thiazolidinones[1–3]

BY IRVING R. SCHMOLKA AND PAUL E. SPOERRI[4]

RECEIVED MARCH 26, 1957

A series of 2-phenyl-3-*n*-alkyl-4-thiazolidinones was prepared and its properties studied. Upon treatment of these compounds with lithium aluminum hydride a reduction of the amide structure with rupture of the thiazolidine ring occurred. The structure of the cleavage product was proved by unequivocal syntheses.

As part of a program to study the effects of varying the heterocyclic ring of a series of quaternary salts, the preparation of N-alkyl-thiazolidines was undertaken. The synthesis of several 2,3-disubstituted-4-thiazolidinones had been reported previously.[5–7] In this paper we report on the synthesis of a series of thiazolidines in which the ring nitrogen was substituted with alkyl groups of increasing lengths. These are listed in Table I.

The products were colorless, ranging from a crystalline to a waxy appearance as the molecular weight increased and were unstable when exposed to sunlight.

The melting points of these compounds show a similar pattern when compared with the melting points of the amides of the aliphatic acid series.

The infrared curves for these compounds show the characteristic absorption bands for a disubstituted amide at 1680 cm.$^{-1}$ and for the thioether at 724 cm.$^{-1}$.

The use of lithium aluminum hydride, according to the reaction conditions of Uffer and Schlittler,[8]

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[1] Part II, *J. Org. Chem.* in press.

[2] Abstracted from the Ph.D. thesis of Irving R. Schmolka, Polytechnic Institute of Brooklyn, June, 1955.

[3] Presented before the Sixth Meeting-in-Miniature of the Metropolitan Long Island Subsection of the American Chemical Society, New York Section, Feb. 25, 1955.

[4] To whom inquiries should be sent.

[5] H. Erlenmeyer and V. Oberlin, *Helv. Chim. Acta*, **30**, 1329 (1947).

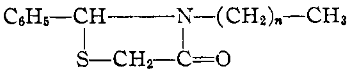
[6] H. D. Troutman and L. M. Long, THIS JOURNAL, **70**, 3436 (1948).

[7] A. R. Surrey, *ibid.*, **69**, 2911 (1947); **70**, 4262 (1948); **71**, 3150 (1949); **71**, 3354 (1949); **74**, 3450 (1952).

[8] A. Uffer and E. Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948).

TABLE I

2-PHENYL-3-*n*-ALKYL-4-THIAZOLIDINONES



$C_6H_5{-}CH{-}N{-}(CH_2)_n{-}CH_3$; $S{-}CH_2{-}C{=}O$

No.	Formula	*n*	M.p., °C.	Yield, %	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
1	$C_{13}H_{17}ONS$	3[a]	57.2–57.7	80	..	..	...	...
2	$C_{15}H_{21}ONS$	5	34.6–35.6	62	5.32	5.21	12.17	12.15
3	$C_{17}H_{25}ONS$	7	61.6–62.6	77	4.81	4.69	11.00	11.10
4	$C_{19}H_{29}ONS$	9	42.0–42.5	74	4.39	4.42	10.03	10.03
5	$C_{21}H_{33}ONS$	11	51.5–52.0	76	4.03	3.92	9.23	9.25
6	$C_{23}H_{37}ONS$	13	57.1–58.1	71	3.73	3.78	8.54	8.60
7	$C_{25}H_{41}ONS$	15	64.8–65.3	67	3.47	3.40	7.94	7.92
8	$C_{27}H_{45}ONS$	17	69.6–70.6	60	3.24	3.18	7.43	7.50

[a] Previously reported by Troutman and Long,[6] m.p. 56.5–57.5°.

seemed to effect the desired conversion of the 4-thiazolidinones to the oxygen-free heterocycles. The 2-phenyl-3-*n*-butyl-4-thiazolidinone, for example, yielded a pale yellow oil which, after purification by vacuum distillation, formed a picrate, a methiodide and a hydrochloride. Similar results were obtained when the method was applied to the reduction of the *n*-octyl, *n*-dodecyl, *n*-tetradecyl and *n*-octadecyl homologs.

In order to prove the assumption that the desired reduction had occurred, it was necessary to synthesize unequivocally 2-phenyl-3-*n*-butylthiazolidine in order to compare it with the reduction product obtained from 2-phenyl-3-*n*-butyl-4-thiazolidinone. Benzylidene-*n*-butylamine[9] was allowed to react with β-mercaptoethanol. Despite a number of variations in reaction conditions, using acidic and basic catalysts, no condensation occurred.

The preparation of 2-phenylthiazolidine[10,11] was effected in 40% yield by condensing benzaldehyde and β-aminoethyl mercaptan. Improved yields (80%) were obtained by adding a cold aqueous solution of the amine hydrochloride to a well-stirred cold alcoholic solution of an excess of benzaldehyde. Only traces of by-product were obtained.

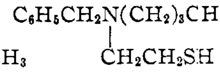
The 2-phenylthiazolidine was then alkylated with *n*-butyl iodide or *n*-butyl *p*-toluenesulfonate. The pale yellow oil isolated in either case differed from the amine obtained by the lithium aluminum hydride reduction in odor, infrared absorption curve and index of refraction. The picrate melted 30° higher than the picrate made from the lithium aluminum hydride reduction product, and the X-ray diffraction pattern was not identical.

Since the possibility that the alkyl group had substituted in the 2-position was not entirely precluded, a further entirely unequivocal synthesis of 2-phenyl-3-*n*-butylthiazolidine was undertaken. The hydrochloride salt of 2-*n*-butylaminoethyl mercaptan[12] was allowed to react with excess benzaldehyde. The isolated oil formed a picrate whose X-ray diffraction pattern was identical with that of the alkylated product previously obtained from 2-phenylthiazolidine. The infrared absorption curves of the free base made by the two methods also proved to be identical. This, of course, demonstrated that the reduction product obtained with lithium aluminum hydride was not the desired thiazolidine.

From an evaluation of the molar refractions (Table II) and infrared data, it seemed likely that the thiazolidine ring had been ruptured, suggesting the probable structure of the compound to be either A or B.

$C_6H_5CH_2SCH_2CH_2NH(CH_2)_3CH_3$

A



$C_6H_5CH_2N(CH_2)_3CH_3$; CH_2CH_2SH

B

TABLE II

MOLAR REFRACTIONS

No.	$n^{25}D$	Density, 25°	Calcd. *MR* ring compd.	*MR* found	Calcd. *MR* split ring[a]
1	1.52324	0.972	68.36	70.23	70.21
3	1.51394	.943	86.84	89.21	88.69
5	1.51022	.931	105.32	107.84	107.17
6	1.50882	.928	114.56	116.97	116.41

[a] Calcd. for split between 1- and 2-atoms. Values for split between 2- and 3-atoms are 0.07 unit greater.

Compound A, N-*n*-butyl-N-(2-benzylmercapto)-ethylamine, was prepared by treating benzyl mercaptan with N-2-chloroethylbutylamine. It could be ruled out as the product by its infrared absorption curve, the melting point of its hydrochloride and the odor of the free base. Compound B, β-(benzyl-*n*-butylamino)-ethyl mercaptan, was made by converting β-(benzyl-*n*-butylamino)-ethyl chloride to the corresponding isothiouronium salt and hydrolyzing it to the mercaptan. The infrared absorption curve of this compound was identical with that of the lithium aluminum hydride reduction product. The respective picrates and methiodides showed no mixed melting point depression. It can be concluded that the lithium aluminum hydride reduction of the 2-phenyl-3-*n*-alkyl-4-thiazolidinones ruptured the thiazolidine ring between the 1- and 2-atoms in addition to reducing the amide to the amine.

The fission of the heterocyclic ring of 2-phenyl-3-*n*-alkyl-4-thiazolidinone between the 1- and 2-

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[9] H. Zaunschirm, *Ann.*, **245**, 279 (1888).

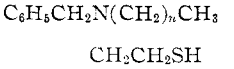
[10] H. T. Clarke, J. R. Johnson and R. Robinson, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 957.

[11] R. Kuhn and F. Drawert, *Ann.*, **590**, 55 (1954), have reported 61% yield.

[12] H. M. Woodburn and B. G. Pautler, *J. Org. Chem.*, **19**, 863 (1954).

TABLE III

β-(BENZYL-*n*-ALKYLAMINO)-ETHYLMERCAPTANS



$C_6H_5CH_2\underset{CH_2CH_2SH}{N}(CH_2)_nCH_3$

Alkyl	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
Butyl	....	$C_{13}H_{21}NS$	69.90	69.86	9.48	9.21	..	..	...	...
Hydrochloride	90.6–91.8	$C_{13}H_{22}NSCl$	...	...	...	...	..	..	12.34	12.63
Octyl	....	$C_{17}H_{29}NS$	73.06	71.81	10.46	10.17	..	..	11.47	11.46
Hydrochloride	77.2–78.2	$C_{17}H_{30}NSCl$	64.62	64.93	9.57	9.78	..	..	..	..
Dodecyl	....	$C_{21}H_{37}NS$	...	...	...	...	4.17	3.93	9.55	9.26
Hydrochloride	63.7–64.7	$C_{21}H_{38}NSCl$	67.81	67.44	10.29	9.93	..	..	8.62	8.70
Tetradecyl	....	$C_{23}H_{41}NS$	75.97	76.13	11.36	11.01	3.85	3.96	...	...
Hydrochloride	67.4–68.9	$C_{23}H_{42}NSCl$	69.04	68.67	10.58	10.20	..	..	8.01	8.29
Octadecyl	37–39	$C_{27}H_{49}NS$	...	...	...	...	..	..	7.64	7.71
Hydrochloride	75.4–76.2	$C_{27}H_{50}NSCl$	71.08	70.74	11.05	11.05	..	..	7.03	7.36

atoms is in agreement with similar results reported for oxazolidines.[13,14]

All the amines from the lithium aluminum hydride reduction appear to be unstable and have an unpleasant odor. The amine hydrochlorides, however, are white, stable compounds. The chemical analyses of the β-(benzyl-*n*-alkylamino)-ethyl mercaptans and their hydrochlorides are shown in Table III.

Experimental[15]

Starting Materials.—The amines used were purified by distillation at atmospheric or reduced pressure, under dry nitrogen. The benzaldehyde was distilled at atmospheric pressure in a dry nitrogen atmosphere, b.p. 179–180°. The commercially available concentrated grade (96–99%) of mercaptoacetic acid[16] was used as received but was stored in the refrigerator to prevent formation of thioglycolide.

2-Phenyl-3-*n*-tetradecyl-4-thiazolidinone.—The preparation of this compound is an example of the general procedure used for the preparation of the compounds listed in Table I and is a modification of that described by Surrey. To a cool solution of 11.0 g. (0.104 mole) of benzaldehyde in 125 ml. of dry benzene was added slowly 22.2 g. (0.104 mole) of freshly distilled *n*-tetradecylamine. The mixture was gently refluxed with a Dean and Stark trap connected to the apparatus. After 1.9 ml. (0.104 mole) of water had collected, 9.7 g. of 97.8% mercaptoacetic acid (0.103 mole) was added dropwise to the pale yellow colored solution, while refluxing, until an additional 1.9 ml. of water was collected. The yellow benzene solution was cooled, washed with dilute sodium carbonate solution to remove unreacted mercaptoacetic acid, with dilute hydrochloric acid to remove unreacted amine and with distilled water until neutral to litmus. The benzene solution was concentrated and the white waxy precipitate was filtered, recrystallized successively from ethyl alcohol, acetone and ether and dried *in vacuo* over calcium chloride. Additional material was recovered from the mother liquor. A yield of 37.0 g. (95.5%) of crude product was obtained which gave 27.5 g. (71%) of a white waxy material, m.p. 57.1–58.1°.

Anal. Calcd. for $C_{23}H_{37}NOS$: S, 8.54; N, 3.73. Found: S, 8.60; N, 3.78.

Lithium Aluminum Hydride Reduction of 2-Phenyl-3-*n*-alkyl-4-thiazolidinones.—In a dry nitrogen atmosphere 100 ml. of anhydrous ethyl ether was added slowly to 20 g. (0.5 mole) of lithium aluminum hydride. With good agitation, a solution of 60 g. (0.255 mole) of 2-phenyl-3-*n*-butyl-4-thiazolidinone in 300 ml. of anhydrous ethyl ether was slowly added at room temperature at such a rate (1.5 hr.) as to maintain a gentle reflux. This was refluxed and agitated for an additional 20 hr. The excess lithium aluminum hydride was decomposed by the dropwise addition of water while maintaining the flask at 0° in an ice-bath. The ether solution was extracted several times with a 20% sodium potassium tartrate solution. The combined ether solutions were concentrated *in vacuo* and the residual oil was dried *in vacuo* over calcium chloride. The pale yellow oil obtained, 40.5 g. (72%), was distilled, and 18.6 g. of a water-white product with an unpleasant odor, b.p. 122–123° at 2 mm., was obtained. It gradually darkened in color until eventually it became a green-black liquid.

A methiodide derivative was obtained by refluxing equimolar quantities in anhydrous ether for 1 hr. The white crystalline precipitate was filtered and recrystallized from absolute ethanol; m.p. 136.0–136.4°.

Anal. Calcd. for $C_{14}H_{24}NSI$: C, 46.03; H, 6.62; N, 3.84. Found: C, 45.79; H, 6.33; N, 3.98.

The picrate was made by melting together equimolar quantities of the amine and picric acid on a steam-bath. Recrystallization from 95% ethanol gave yellow-orange crystals, m.p. 92.3–93.3°.

Anal. Calcd. for $C_{19}H_{24}N_4O_7S$: N, 12.39; S, 7.09. Found: N, 12.22; S, 7.09.

When the lithium aluminum hydride reduction was applied to the higher molecular weight homologs, the combined ether extracts were treated with dilute hydrochloric acid solution. The lower aqueous layers were separated and dried *in vacuo*. The residues were washed with ether, recrystallized from acetone and stored. Attempts to purify the free bases by vacuum distillation were not successful, resulting in extensive decomposition. Thus, the *n*-octadecyl compound was a pale yellow oil which, upon standing in the dark, gradually changed to a white waxy solid. But the distillate from this material was an orange waxy solid.

2-Phenylthiazolidine.—Commercially available ethyleneimine[17] was used to prepare β-mercaptoethylamine hydrochloride, following the method of Mills and Bogert.[18] Of the several methods tried, the following was found to give the highest yields: A cool solution of 18 g. (0.15 mole) of β-mercaptoethylamine hydrochloride in 100 ml. of water was added slowly over a period of 15 minutes with vigorous agitation to a cool solution of 50 g. (0.47 mole) of benzaldehyde in 135 g. of 70% ethanol. The mixing was continued another 15 minutes after addition was complete, and the mixture was stored in the refrigerator overnight. The alcohol was evaporated and the excess benzaldehyde extracted with ether. The acid solution was made alkaline by the slow addition, with vigorous stirring, of powdered potassium carbonate. The white crystalline precipitate was filtered, washed with water, filtered and air-dried. The product was purified by vacuum sublimation at 80–90° (2 mm.). There was obtained 20.6 g. (78.5%) of white crystals, m.p. 108.3–108.8°, reported m.p. 105–109°,[10] 109–110°.[11]

The compound was further characterized by the following derivatives, made by standard procedures:

Picrate, m.p. 136.3–137.3°. *Anal.* Calcd. for $C_{15}H_{14}N_4O_7S$: S, 8.13. Found: S, 7.84.

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[13] H. Heusser, P. T. Herzig, A. Furst and P. A. Plattner, *Helv. Chim. Acta*, **33**, 1093 (1950).

[14] E. D. Bergman, D. Lavie and S. Pinchas, THIS JOURNAL, **73**, 5662 (1951).

[15] All melting points are corrected, boiling points are not. Analyses by Dr. K. Ritter, Zurich, Switzerland, and the Analytical Division of the Research and Development Department of the Colgate Palmolive Co.

[16] Evans Chemetics, Inc., New York, N. Y.

[17] Chemirad Corporation, Port Washington, L. I., N. Y.

[18] E. J. Mills, Jr., and M. T. Bogert, THIS JOURNAL, **62**, 1177 (1940).

Acetamide, m.p. 64.3–64.8°. *Anal.* Calcd. for $C_{11}H_{13}NOS$: S, 15.46. Found: S, 15.75.

Hydrochloride, m.p. 202.4–202.9° dec. *Anal.* Calcd. for $C_9H_{12}NSCl$: S, 15.89. Found: S, 15.96.

Benzenesulfonamide, m.p. 131.4–131.9°. *Anal.* Calcd. for $C_{15}H_{15}NO_2S$: S, 21.00. Found: S, 21.18.

2-*n*-Hexylthiazolidine.—The previously described method was used to prepare 2-*n*-hexylthiazolidine in 84% yield, b.p. 76–77° at 2 mm., $n^{25}\text{D}$ 1.49597. The product, a water-white liquid with a mild unpleasant odor, slowly decomposed upon aging.

Anal. Calcd. for $C_9H_{19}NS$: C, 62.37; H, 11.05; N, 8.08. Found: C, 62.54; H, 11.11; N, 8.07.

The picrate was recrystallized from 95% ethanol; m.p. 134.8–135.3°.

Anal. Calcd. for $C_{15}H_{22}N_4SO_7$: C, 44.77; H, 5.51. Found: C, 44.52; H, 5.34.

2-*n*-Octylthiazolidine.—The same method was used to prepare this compound, isolated as its hydrochloride, in 88.5% yield. After recrystallization from 95% ethanol, a white crystalline material with a pleasant odor was obtained; m.p. 103.0–103.5°.

Anal. Calcd. for $C_{11}H_{24}NSCl$: C, 55.55; H, 10.17; N, 5.89. Found: C, 55.63; H, 10.28; N, 5.75.

The free base, prepared from its salt, was purified by vacuum distillation; b.p. 92–94° at 1.5 mm., $n^{25}\text{D}$ 1.49179, and had a pleasant odor. The infrared absorption curve of the base, resembling that of the *n*-hexyl homolog, exhibits the absorption bands for the thioether group at 722 cm.$^{-1}$ and for a secondary amine at 3270 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{23}NS$: C, 65.61; H, 11.51. Found: C, 65.33; H, 11.46.

The picrate was recrystallized from 95% ethanol; m.p. 143.9–144.9°.

2-Phenyl-3-*n*-butylthiazolidine. Method A.—To a mixture of 1.9 g. (0.018 mole) of anhydrous sodium carbonate and 25 ml. of anhydrous ethyl alcohol were added 2.7 g. (0.16 mole) of 2-phenylthiazolidine and 3.0 g. (0.016 mole) of *n*-butyl iodide. The mixture was refluxed gently for 14 hr. After cooling to room temperature, the alcoholic solution was filtered and the filtrate evaporated. A pale yellow oil and a white solid, obtained as the residue, were separated by filtering. The residue was washed with water and 0.8 g. of the starting 2-phenylthiazolidine was recovered. The pale yellow oil weighed 2.5 g. (96%) and had a mild unpleasant odor, $n^{25}\text{D}$ 1.54970.

The picrate was recrystallized from 95% ethanol; m.p. 120.6–121.6°.

Anal. Calcd. for $C_{16}H_{22}N_4O_7S$: C, 50.66; H, 4.92; N, 12.44; S, 7.12. Found: C, 50.71; H, 4.55; N, 12.32; S, 7.17.

When the alkylation was carried out with *n*-butyl *p*-toluenesulfonate,[19] the same product was obtained and the picrate showed no depression in a mixed melting point.

2-*n*-Butylaminoethyl Mercaptan.—Into a solution of 20 g. (0.274 mole) of *n*-butylamine in 100 ml. of anhydrous ether was added slowly 5.7 g. (0.095 mole) of freshly distilled ethylene sulfide.[20] The contents were left at room temperature for 4 days. The ether and excess *n*-butylamine were removed *in vacuo* and the residual oil vacuum distilled. There was obtained 3.5 g. (28%) of 2-*n*-butylaminoethylmercaptan, a colorless liquid, b.p. 84–85° at 19 mm.[12]

2-Phenyl-3-*n*-butylthiazolidine. Method B.—Into a beaker containing 26 meq. of hydrochloric acid in 100 ml. of water was added slowly 3.5 g. (0.026 mole) of 2-*n*-butylaminoethylmercaptan. This solution was cooled and then slowly added with good agitation to a cold solution of 10 g. (0.095 mole) of benzaldehyde in 100 ml. of 95% ethanol. The mixture was stirred an additional 15 minutes and placed in the refrigerator overnight. The solution was concentrated and the alcohol-free concentrated solution was extracted with ether to remove excess benzaldehyde. The free base was liberated by the addition of anhydrous potassium carbonate. There was obtained 4.0 g. (69%) of a pale yellow oil of a mild unpleasant odor, $n^{25}\text{D}$ 1.54958. It was distilled *in vacuo* and a water-white liquid was obtained, b.p. 104–106° at 2 mm., $n^{25}\text{D}$ 1.55242, d^{25}_4 1.026, $M\text{D}$ 68.98 (calcd. 68.36).

Anal. Calcd. for $C_{13}H_{19}NS$: C, 70.53; H, 8.66. Found: C, 70.36; H, 8.41.

The infrared absorption curves of the two compounds made by the two methods showed them to be identical; the absorption band for the thioether group is at 728 cm.$^{-1}$.

It formed a picrate which was identical (mixed m.p.) with the one obtained from method A.

N-2-Chloroethyl-butylamine Hydrochloride.—The free base was prepared[21] and isolated as the hydrochloride. It was recrystallized from acetone, and a 70% yield of white crystals, m.p. 237.2–237.8° dec., was obtained.

Anal. Calcd. for $C_6H_{15}NCl_2$: C, 41.87; H, 8.79. Found: C, 41.98; H, 9.04.

N-*n*-Butyl-N-(2-benzylmercapto)-ethylamine.—To 23 g. (0.185 mole) of benzyl mercaptan in a dry nitrogen atmosphere was added 100 ml. of 95% ethanol and a solution of 15.5 g. (0.38 mole) of 98.5% sodium hydroxide in 150 ml. of 95% ethanol. The flask was immersed in an ice-bath. A solution of 31.6 g. (0.185 mole) of N-2-chloroethylbutylamine hydrochloride in 250 ml. of 95% ethanol was added dropwise over a period of 30 minutes, with agitation. It then was refluxed gently for 2.5 hr. and allowed to stand overnight. The alcohol was removed under reduced pressure. Water was added to the residue and the pink oil obtained was extracted several times with ether and the aqueous layer discarded. The ether solution was extracted several times with dilute hydrochloric acid. The aqueous amine hydrochloride solution was concentrated and a white crystalline precipitate was obtained. Upon filtration and recrystallization from acetone, there was obtained 29.1 g. (60.5%) of the amine hydrochloride, m.p. 164.4–164.9°.

Anal. Calcd. for $C_{13}H_{22}SNCl$: C, 60.09; H, 8.54; N, 5.39. Found: C, 60.01; H, 8.41; N, 5.28.

The free base boiled at 110–112° at 1.5 mm., d^{25}_4 0.980, n^{25}_4 1.53082, $M\text{D}$ 70.50 (calcd. 70.37).

β-(Benzyl-*n*-butylamino)-ethyl Chloride Hydrochloride.—The free base[22] was converted to the white crystalline hydrochloride salt; yield 67 g. (76.5%), m.p. 93.1–94.1°.

Anal. Calcd. for $C_{13}H_{21}NCl_2$: C, 59.54; H, 8.07. Found: C, 59.70; H, 8.21.

β-(Benzyl-*n*-butylamino)-ethylisothiouronium Chloride Hydrochloride.—The method of converting an amine chloride hydrochloride recommended by Albertson and Clinton[23] was followed. To a solution of 19.5 g. (0.255 mole) of thiourea in 75 ml. of anhydrous ethanol, a solution of 66 g. (0.25 mole) of β-(benzyl-*n*-butylamino)-ethyl chloride hydrochloride in 200 ml. of anhydrous ethanol slowly was added over a period of 30 minutes. The resulting solution was refluxed for 6 hr., cooled in ice and diluted with a mixture of 500 ml. of ethyl acetate and 150 ml. of Skelly A. The precipitate was filtered, air-dried and recrystallized from an alcohol–ether mixture. There was obtained 69 g. (81%) of a dry white powder, m.p. 162.9–163.9°.

Anal. Calcd. for $C_{14}H_{25}N_3SCl_2$: C, 49.69; H, 7.45. Found: C, 49.78; H, 7.73.

β-(Benzyl-*n*-butylamino)-ethyl Mercaptan.—To 68 g. (0.20 mole) of β-(benzyl-*n*-butylamino)-ethylisothiouronium chloride hydrochloride suspended in 100 ml. of water was added a warm, freshly prepared solution of 17 g. of 47.0% sodium hydroxide (0.20 mole) in 60 ml. of water. An immediate separation of a pink upper oily layer occurred. The mixture was saturated with salt and extracted with three 50-ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate, filtered and the ether solution was distilled in a stream of dry nitrogen. The residual liquid was distilled under dry nitrogen and 31.5 g. (74%) of a colorless liquid, b.p. 132–134° at 3 mm., was obtained; $n^{25}\text{D}$ 1.52324, d^{25}_4 0.972, $M\text{D}$ 70.31 (calcd. 70.21). The infrared absorption curve showed weak absorption bands at 909 and at 2540 cm.$^{-1}$, indicating the presence of the mercaptan group.

A picrate and a methiodide were prepared and were identical with those obtained from the lithium aluminum hydride reduction of 2-phenyl-3-*n*-butyl-4-thiazolidinone.

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

Amine Oxides. III. Selective Formation of Olefins from Unsymmetrical Amine Oxides and Quaternary Ammonium Hydroxides[1]

BY ARTHUR C. COPE, NORMAN A. LEBEL,[2] HIOK-HUANG LEE[3] AND WILLIAM R. MOORE

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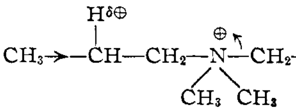
The relative amounts of olefins formed in the thermal decomposition of unsymmetrical amine oxides and structurally related quaternary ammonium hydroxides, $R_1R_2MeN^{\oplus}{-}O^{\ominus}$ and $R_1R_2Me_2N^{\oplus}OH^{\ominus}$, have been determined. The ratios of olefins obtained from the amine oxides are affected less by the structures of the alkyl groups than are the ratios of olefins formed from the quaternary bases, and roughly approximate the ratios of the numbers of β-hydrogen atoms in the alkyl groups. This result is interpreted as being caused by smaller steric effects in the five-membered cyclic transition state for amine oxides than in the planar *trans* transition state leading from quaternary bases to olefins. An order of decreasing ease of elimination of alkyl groups as olefins, corrected for the number of available β-hydrogen atoms, for amine oxides is: β-phenylethyl ≫ *t*-butyl > isobutyl ∼ isopropyl ∼ *n*-decyl > *n*-butyl > isoamyl > ethyl > *n*-propyl. For quaternary ammonium bases the order is β-phenylethyl ≫ *t*-butyl > ethyl > isopropyl ≫ *n*-propyl > isobutyl ∼ *n*-decyl ∼ *n*-butyl > isoamyl.

A number of proposals have been advanced to explain the relative amounts of olefins formed in bimolecular elimination reactions. Secondary or tertiary halides undergo elimination to produce the most highly alkylated olefin according to the Saytzeff rule.[4] Hyperconjugative stabilization of the incipient double bond in the transition state leading to the most highly alkylated olefin has been accepted generally as explaining eliminations that proceed by the Saytzeff rule,[5] forming the thermodynamically more stable products.[6]

In the bimolecular eliminations of quaternary ammonium ions (also sulfonium ions), which follow the Hofmann rule,[7,8] other factors must be considered to explain the production of the least highly alkylated, *i.e.*, less stable, olefin. The English workers attribute this directive influence to an inductive effect, brought about by the presence of the unit positive ionic charge in these compounds.[5] The induced positive character of the β-carbon atoms is partially neutralized by an electron-releasing alkyl group (methyl in I, below), causing the β-protons to be less susceptible to attack by base in this alkyl branch. Because of this inductive effect, the terminal methyl group in the *n*-propyl chain (I) acts to suppress propylene formation if elimination can produce ethylene. In support of the above explanation, the relative ease of olefin formation from the decompositions of quaternary ammonium hydroxides has been determined by comparing the yields of olefins from quaternary bases containing only one olefin-yielding alkyl group, and otherwise methyl groups.[8]



$$\underset{\displaystyle CH_3\quad CH_3}{CH_3 \rightarrow \overset{H^{\delta\oplus}}{CH} - CH_2 - \overset{\oplus}{N} - CH_2 - \overset{H^{\delta\oplus}}{CH} - H}$$

I

A study of the competitive formation of different olefins from a series of quaternary ammonium hydroxides of the type $(RCH_2CH_2)_2N^{\oplus}(CH_2CH_2R')_2\text{-}OH^{\ominus}$ and some related types has been reported.[9] The observed ratios of olefins formed, statistically corrected for the number of β-hydrogen atoms present, were concluded to be influenced primarily by the electrical properties of the groups R and R′, with steric effects (hindrance to attack by the base) being important only in cases where R or R′ is *t*-butyl.

trans-Stereospecificity has been firmly established for bimolecular elimination reactions[10] if such a reaction course is possible. Steric control of bimolecular elimination reactions of quaternary bases has been proposed by Schramm,[11] who represented the transition states with unlikely configurations. Brown and co-workers, who previously had observed a Hofmann-type elimination in the solvolysis of a tertiary chloride,[12] doubted that the directive influence in elimination reactions following the Hofmann rule necessarily resulted from the presence of a positive charge on the group being eliminated.[13] An increase in the steric requirements (size) of the β-alkyl group or groups,[14a] the base[14b] and the leaving group[14c] has been shown to cause

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