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Mercaptoethylation. I. Mercaptoethylation of Amines with Ethylene Monothiolcarbonate

D. D. REYNOLDS, MARY K. MASSAD, D. L. FIELDS, and D. L. JOHNSON

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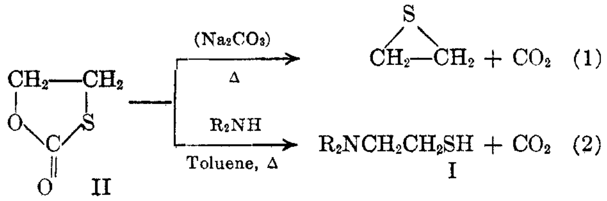
Ethylene monothiolcarbonate is shown to be a convenient reagent for the mercaptoethylation of moderately to strongly basic primary and secondary amines. The yields of the 2-aminoethanethiols thus produced compare favorably with reported yields obtained by reaction of an amine with ethylene sulfide.

Hitherto interest in *N*-substituted 2-aminoethanethiols (I) has centered primarily in the pharmaceutical and synthetic-rubber industries.[1] Their value as synthetic intermediates, as well as their potential application to photography, suggested an investigation of new methods for their preparation. A survey of the literature indicated three procedures[2-4] commonly used. Two of the procedures employ the corresponding 2-aminoethyl halide as a precursor—*i.e.*, its reaction with hydrosulfides of alkali metals[2] and its reaction with thiourea followed by alkaline hydrolysis.[3] The third and more attractive general route to 2-aminoethanethiols has been a one-step reaction of primary and secondary amines with ethylene sulfide.[4] The main disadvantage of the latter preparation is the necessity of isolating and handling the low-boiling, readily polymerizable ethylene sulfide.[5] Recently one of the authors[6] disclosed a new synthesis of ethylene sulfide by the base-catalyzed decomposition of the now commercially available ethylene monothiolcarbonate (II) (Eq. 1). The ease of this preparation suggested the possibility of the reaction of II with primary and secondary amines to form I without prior isolation of the ethylene sulfide (Eq. 2).



This possibility was realized for moderately to strongly basic organic amines. The results obtained for a few representative examples are tabulated in Table I. The experimental procedure involved overnight refluxing of II with a two-molar excess of amine in a nonpolar solvent such as benzene or toluene. The smooth evolution of carbon dioxide was usually completed in the early phase of the reaction and an additional reaction period was employed to ensure a complete reaction of the *in situ*-generated ethylene sulfide. The product was isolated in each case by distillation.

Although the yields obtained are comparable to the reported yields derived by the direct reaction of ethylene sulfide with the amine (see Table I), the procedure described is much more readily amenable to large-scale production than would be possible with ethylene sulfide. The principal side reaction of this preparation is further mercaptoethylation of the aminoethanethiols to yield compounds of structure III (Equation 3), the extent of this reaction being governed by the relative nucleophilicities and concentrations of the amine and the newly produced thiols. Such side reactions are usually suppressed by increasing the ratio of amine to II as well as by increasing the amount of solvent in order to retain nonpolar reaction conditions.

$$R_2NCH_2CH_2SH + n\mathrm{II} \longrightarrow \underset{\mathrm{III}}{R_2N(CH_2CH_2S)_{n+1}H} + nCO_2 \quad (3)$$

The lower yield observed for the attempted monomercaptoethylation of primary amines (Table I, Nos. 6–9), compared with that for secondary amines (Table I, Nos. 1–5), is attributed to bismercaptoethylation of the amine as well as to the aforementioned mercaptoethylation of mercaptan (Equation 3). Interestingly, when an attempt was made to bismercaptoethylate several primary amines—*i.e.*, *n*-butyl-, allyl-, and cyclohexylamines—by reaction of two moles of II per mole of amine following Equation (4), no desired bis(2-mercaptoethyl)amine (IV) was obtained. Instead, *n*-butyl- and allylamines yielded 55 and 54% of their respective 2-

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[1] For leading references, see E. E. Reid, *Organic Chemistry of Bivalent Sulfur*, Vol. I, Chemical Publishing Co., Inc., New York, N. Y., 1958, p. 400.

[2] (a) N. F. Albertson and R. O. Clinton, *J. Am. Chem. Soc.*, **67**, 1222 (1945). (b) H. Gilman, M. A. Plunkett, L. Tolman, L. Fullhart, and H. S. Broadbent, *J. Am. Chem. Soc.*, **67**, 1845 (1945). (c) B. Tchoubar, *Bull. soc. chim. de France* (*Mémoires*), (5) 14, 792 (1947).

[3] (a) R. O. Clinton, V. J. Salvador, S. C. Laskowski, and C. M. Suter, *J. Am. Chem. Soc.*, **70**, 950 (1948). (b) J. Harley-Mason, *J. Chem. Soc.*, 320 (1947).

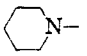
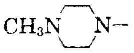
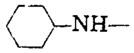
[4] (a) W. Reppe and F. Nicolai, Ger. Patent **631,016** (1936); *Chem. Abstr.*, **30**, 6008 (1936). (b) H. R. Snyder, J. M. Stewart, and J. B. Ziegler, *J. Am. Chem. Soc.*, **69**, 2672 (1947). (c) G. I. Braz, *Zhur. Obshcheĭ Khim. S.S.S.R.*, 21, 688 (1951). (d) Y. K. Yuryev and L. S. German, *News Moscow State Univ., Phys. Chem. Ser.*, No. 1, 197 (1956); *Chem. Abstr.*, **52**, 9069 (1958).

[5] For a review of the chemistry of ethylene sulfide through 1948, see C. C. J. Culvenor, W. Davies, and N. S. Heath, *J. Chem. Soc.*, 282 (1949).

[6] D. D. Reynolds, *J. Am. Chem. Soc.*, **79**, 4951 (1957).

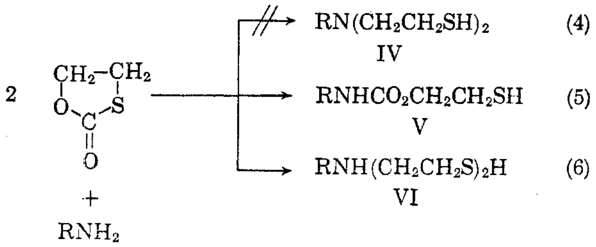
TABLE I

2-AMINOETHANETHIOLS
$R_2NCH_2CH_2SH$

No.	R_2N—	B.P./ Mm.[a]	n_D^{25}	Yield, %	Purity, %[l]	Calcd., % C	Calcd., % H	Calcd., % N	Calcd., % S	Found, % C	Found, % H	Found, % N	Found, % S
1		83/11 85/11[b]	1.5000 1.4995[b]	76 77[i]	97	58.0	10.4	9.7	22.1	57.9	10.5	9.7	21.5
2		92/10 101/15[b]	1.5025 1.5030[b]	68 83[j]	98	49.1	8.9	9.5	21.8	48.8	9.2	9.4	21.4
3		95/10	1.5045	63	98	52.5	10.0	17.5	20.0	52.7	10.1	17.1	19.8
4	$(C_2H_5)_2N$—	72/29 65/23[c]	1.4632 1.4680[f]	51 80[j]	99	54.3	11.4	10.5	24.1	54.1	11.3	10.3	23.9
5	$(n\text{-}C_4H_9)_2N$—	66/0.7 74/2[d]	1.4622 1.4635[g]	81 70–80[i]	99	63.6	12.1	7.4	16.9	64.0	12.5	7.2	17.2
6	$n\text{-}C_4H_9NH$—	47/0.1	1.4713	10	94	54.3	11.4	10.5	24.1	54.3	11.3	10.1	24.3
7	$n\text{-}C_6H_{13}NH$—	76/1.5 103/9[e]	1.4681 1.4700[h]	47 58[j]	100	59.7	11.9	8.7	19.9	60.0	11.8	8.3	19.9
8	$C_6H_5CH_2NH$—	101/0.7 124/6[e]	1.5598 1.6057[h]	61 68[j]	99	64.8	7.9	8.5	19.2	64.8	7.9	8.2	19.2
9		77/0.5	1.5042	33	99	60.8	10.2	8.9	20.2	60.4	10.6	9.1	19.9
10	C_6H_5NH—	—	—	0[k]									

[a] Boiling points are uncorrected. [b] Ref. 3a. [c] Ref. 2a. [d] Ref. 4b. [e] Ref. 4c. [f] Ref. 2a, n_D^{20}. [g] Ref. 4b, n_D^{20}. [h] Ref. 4c, n_D^{20}. [i] Ref. 4b, prepared by reaction of ethylene sulfide with the amine. [j] Ref. 4c, crude yield; prepared by reaction of ethylene sulfide with the amine. [k] Starting materials were completely recovered. [l] Determined by iodometric titration.

mercaptoethyl carbamates (V, R = n-C_4H_9—, CH_2=$CHCH_2$—)[7] as the only distillable products, while a 53% yield of 2-(2-cyclohexylaminoethylmercapto)ethanethiol (VI, R = C_6H_{11}—) was obtained from cyclohexylamine.



The remaining yields in all cases were made up of high-boiling higher mercaptoethylated products.

The structures of all new compounds described in this paper were assigned on the basis of elemental analysis and iodometric titration of mercaptan.

EXPERIMENTAL

Materials. Ethylene monothiolcarbonate, n_D^{25} 1.5102, was purchased from Distillation Products Industries, Rochester, N. Y. The amines and solvents were dried by distillation over calcium hydride.

General mercaptoethylation procedures. (a) Monomercaptoethylation. Three moles of a primary or secondary amine was refluxed with 500 ml. of anhydrous toluene under an efficient condenser. Ethylene monothiolcarbonate (1 mole, 104 g.) was then added dropwise to the reaction mixture over a 15-min. period. Refluxing was continued for 15 hr. The cooled solution was washed with two 100-ml. portions of water, dried over anhydrous magnesium sulfate, and distilled under reduced pressure through a 14-in., glass-helices-packed column equipped with a variable-reflux-ratio head.

(b) *Attempted bismercaptoethylation of primary amines.* The preparation of bis(2-mercaptoethyl) derivatives of n-butyl-, allyl-, and cyclohexylamines was attempted by an analogous procedure except that 2 moles of ethylene monothiolcarbonate was used for each mole of amine. The only products characterized from these reactions were as follows:

From n-butylamine there was obtained 97 g. (55%) of product V, R = n-C_4H_9, b.p. 111°/0.06 mm., n_D^{25} 1.4809, 95% pure.

Anal. Calcd. for $C_7H_{15}NO_2S$: C, 47.5; H, 8.5; N, 7.9; S, 18.1. Found: C, 47.6; H, 9.0; N, 8.3; S, 18.1.

Similarly from allylamine there was obtained 87 g. (54%) of product V, R = CH_2=$CHCH_2$—, b.p. 97°/0.06 mm., n_D^{25} 1.4994, 95% pure.

Anal. Calcd. for $C_6H_{11}NO_2S$: C, 44.7; H, 6.8; N, 8.7. Found: C, 44.8; H, 7.4; N, 8.5.

An amount of 116 g. (53%) of VI, R = C_6H_{11}—, b.p. 154°/1.0 mm., n_D^{25} 1.5352, 99% pure, was the only product isolated from cyclohexylamine.

Anal. Calcd. for $C_{10}H_{21}NS_2$: C, 55.0; H, 9.2; N, 6.3; S, 29.3. Found: C, 55.1; H, 9.6; N, 6.4; S, 28.9.

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[7] For the preparation and reactions of a series of these 2-mercaptoethyl carbamates, see (a) D. D. Reynolds, D. L. Fields, and D. C. Johnson, *J. Org, Chem.*, **26**, 5111 (1961), Part II of this series; (b) D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.*, **26**, 5116 (1961), Part III of this series.