BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 39 917—920 (1966)

A Preliminary Study of the Carboxylation and Decarboxylation of Some Sulfides[1)]

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(Received September 3, 1965)

Some sulfides with benzylic hydrogen have been carboxylated by carbonating the respective carbanions generated with dimsylsodium in dimethyl sulfoxide. The resulting mercaptocarboxylic acids have then been found to have considerably-enhanced rates of decarboxylation reaction.

The ability of divalent sulfide groups to stabilize the α-carbanion has been disclosed in a number of reactions.[2)] The Dieckmann condensation of α, β-dicarboxy methyl ethyl sulfide, the tautomeric double-bond migration between vinyl and allyl sulfides, the alkylation at the α-carbon of mercaptal, and the hydrogen isotopic exchange reaction, are a few typical examples of these reactions. Recently we have suggested that the electron-accepting 3d orbital resonance of the divalent sulfur atom is the major factor in the facile base-catalyzed D–H hydrogen isotopic exchange reactions of a number of mercaptals and related compounds.[2b,3)]

$$\mathrm{R}\text{-}\underset{\cdot\cdot}{\ddot{\mathrm{S}}}\text{-}\overset{\ominus}{\underset{|}{\mathrm{C}}}\text{-} \leftrightarrow \mathrm{R}\text{-}\overset{\ominus}{\underset{\cdot\cdot}{\ddot{\mathrm{S}}}}{=}\underset{|}{\mathrm{C}}\text{-} \tag{1}$$

Base-catalyzed decarboxylation is also considered to be a reaction involving the carbanion intermediate which is similar to the base-catalyzed hydrogen exchange reaction.[4)] However, no systematic investigation of the decarboxylation reaction of α-substituted mercapto-carboxylic acids has been known. If the carbanion is relatively stable and if, hence, its equilibium concentration is substantial in a basic solution, it would not be difficult to trap the carbanion by reacting it with carbon dioxide. In the case of the hydrogen exchange or the decarboxylation reaction, a rapid reaction does not necessarily mean a high equilibrium concentration of carbanion. Only a few examples are known which indicate an appreciable concentration of the carbanion of divalent sulfide in an equilibrating system. Fröling and Arens found that mercaptals were metalated in liquid ammonia, and they observed an increased electrical conductivity in the reaction mixture.[5)] Truce and Roberts found that benzaldehyde diphenylmercaptal was readily metalated in dimethylformamide, and that the resulting carbanion was alkylated with alkyl halide.[6)] Therefore, the study of the decarboxylation of mercapto-carboxylic acids and the carboxylation of sulfides is quite significant for the evaluation of the effects of the divalent sulfide group on the stabilization of the carbanion.

$$\mathrm{R}\text{-}\underset{\cdot\cdot}{\ddot{\mathrm{S}}}\text{-}\overset{|}{\underset{|}{\mathrm{C}}}\text{-}\mathrm{CO_2}^{\ominus} \rightarrow \mathrm{R}\text{-}\underset{\cdot\cdot}{\ddot{\mathrm{S}}}\text{-}\overset{\ominus}{\underset{|}{\mathrm{C}}}\text{-} + \mathrm{CO_2} \tag{2}$$

$$\mathrm{R}\text{-}\underset{\cdot\cdot}{\ddot{\mathrm{S}}}\text{-}\overset{\ominus}{\underset{|}{\mathrm{C}}}\text{-} + \mathrm{BH}^{\oplus} \rightarrow \mathrm{R}\text{-}\underset{\cdot\cdot}{\ddot{\mathrm{S}}}\text{-}\overset{|}{\underset{|}{\mathrm{C}}}\text{-H} + \mathrm{B} \tag{3}$$

During the course of the investigations aimed at finding some appropriate base and solvent systems for the generation of carbanions of various sulfides at an appreciable equilibrium concentration, we have found that some sulfides with benzylic hydrogen can be successfully carboxylated by quenching, with carbon dioxide, solutions of the sulfides in dimsylsodium - dimethyl sulfoxide. The resulting carboxylic acids have all been found to have enhanced rates of decarboxylation. This paper will describe the preliminary results of these carboxylation and decarboxylation reactions.

Results and Discussion

Carboxylation Reactions.—A sulfide was dissolved in an excess of 0.5 N dimsylsodium in dimethyl sulfoxide[7)] under an air-free nitrogen atmosphere. When a sulfide was dissolved, the initial brilliant red color of the dimsylsodium solution due to the addition of an indicator amount of triphenylmethane turned a dark yellowish brown, dark green, or dark purple depending on the kind of sulfide dissolved.

[1)] a) Paper VIII: 3d-Orbital Resonance in Divalent Sulfides. b) This work was supported by the Petroleum Research Fund, administered by the American Chemical Society.

[2)] a) C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York (1962); b) S. Oae, "3d Orbital Resonance Involving the Sulfur Atoms in Organic Sulfides," in "Organic Sulfur Compounds," Ed. by N. Kharasch, Vol. IV, Pergamon Press, in press.

[3)] S. Oae, W. Tagaki and A. Ohno, *Tetrahedron*, **20**, 427 (1964), and the preceding papers.

[4)] a) B. R. Brown, *Quart. Revs.*, **5**, 137 (1951); b) J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill, New York, (1962).

[5)] A. Fröling and J. F. Arens, *Rec. trav. chim.*, **81**, 1009 (1962).

[6)] W. E. Truce and F. E. Roberts, *J. Org. Chem.*, **28**, 961 (1963).

[7)] E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 866 (1962).

The carboxylation was then performed by quenching the reaction mixture with or an ether suspension of solid carbon dioxide. The results are shown in Table I.

As is indicated in Table I, none of the carboxylic acids were obtained from the sulfides, VI and VII, with only the aliphatic C–S bonds. In the case of 1, 3-dithian (VI), the starting sulfides was largely recovered alone with a small amount of resinous product. The bicyclic sulfide (VII) also gave mainly a resinous product. These resinous products were probably formed by the cleavage of C–S bonds, similar to the cases where mercaptals were cleaved by some such metalating agents as Grignard reagents, phenyllithium, or *n*-butyllithium.[2a,8,9]

Although qualitative, it seems that the yield of the carboxylic acid in Table I can be explained on the basis of the stability of the carbanion formed by the dissociation of the α-proton of sulfide. The rates of hydrogen exchange reaction have been found to increase dramatically with the increase in the number of the substitution of the mercapto group at the α-carbon atom.[3] Similarly, Table I indicates that the yield of the carboxylic acid from benzaldehyde diethylmercaptal (II) is much higher than that from the benzyl ethyl sulfide (I). Table I also indicates that the yield of the carboxylic acid from benzyl phenyl sulfide (III) is much higher than that from benzyl ethyl sulfide (I). This appears to indicate that the phenylmercapto group is more effective than the ethylmercapto group in the stabilization of carbanion, this is confirmed by the results of the subsequent decarboxylation reactions shown in Table II.

Decarboxylation Reaction.—As Table I shows, the acids, XII and XI, obtained from the sulfides, II and IV, were readily decomposed when their crystals were heated at around 140°C in a glass tube, there was also a vigorous evolution of carbon dioxide. The corresponding sulfides, II and IV, were quantitatively obtained. The acids from the III and V sulfides, are relatively stable, and their decomposition was not observed below 200°C. These acids were then subjected to the base-catalyzed decarboxylation reaction. The results are shown in Table II, although the methods of the kinetics will be reported in detail elsewhere.

Table II appears to disclose the following three points: (1) The rate of diethyl mercapto acetic acid (VIII) is much smaller than those of the other acids. (2) The rates of the decarboxylation of the disubstituted acids, IX and X, are smaller than those of the trisubstituted acids, XI and XII. (3) The rates of the decarboxylation of phenylmercapto-substituted acids (XI and IX) are greater than that of ethylmercapto-substituted acids, (XII and VIII). These observations can be explained by assuming that the ability to stabilize α-carbanion is greater for phenyl and phenylmercapto groups than for the aliphatic mercapto (RS) group, and that the stability of the carbanion is increased with the increasing substitution of mercapto groups.

The products of the decarboxylation reaction were analyzed, the results are shown in Table III. The most plausible mechanism for the present decarboxylation reaction is the formation of carbanion at the rate determining slow step, followed by the fast protonation of the carbanion. However, such other mechanisms as the formation of a methylene intermediate are also possible, in which different kinds of products may be expected.[10] Although the analyses were preliminary and were not thoroughly enough to exclude the formation of a very small quantity of unknown products, it was found that more than 90% of the mercapto acids were decomposed to give carbon dioxide and that the corresponding mercaptals were obtained in high yields; the direct analyses of the reaction mixtures by gas chromatography did not indicate the formation of products other than dimethyl sulfoxide and the mercaptals. The products of the decomposition of diphenoxyacetic acid other than carbon dioxide are not clear. The infrared spectra of the product, however, showed the presence of phenol. This suggests a possibility that the mechanism of the decarboxylation of RO-substituted acid is different from that of RS-substituted acetic acids.

Experimental

The Preparation of Sulfides.—Benzyl ethyl sulfide (I) and benzyl phenyl sulfide (III) were prepared by the reaction of benzyl chloride with the corresponding sodium mercaptide in ethanol (I, b. p. 110°C/20 mmHg; II, b. p. 167—168°C/15 mmHg, m. p. 40—42°C). Benzaldehyde diphenylmercaptal (IV) was prepared by saturating the mixture of benzaldehyde and phenyl mercaptan with dry hydrogen chloride (b. p. 183—184°C/1 mmHg; m. p. 50—51°C). Similarly, formaldehyde diphenylmercaptal (V) was prepared by the acid (HCl)-catalyzed condensation of formaldehyde with phenylmercaptan (b. p. 164—167°C/3 mmHg). The preparations and the properties of benzaldehyde diethylmercaptal (II) and the cyclic mercaptals, VI and VII, have been reported in previous papers.[11]

Carboxylation Reaction.—Commercial dimethyl sulfoxide was dried with calcium hydride under 50°C and vacuum-distilled (below b. p. 55°C). Sodium hydride (7 g.) in a 50% oily suspension was dissolved in 590 ml. of the above dimethyl sulfoxide below 60°C under an air-free nitrogen atomosphere to give a pale brown dimsylsodium solution,[7] the solution was then

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[8] E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. III, Chemical Publishing Co., New York, N. Y. (1960), p. 332.

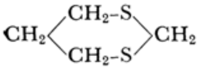
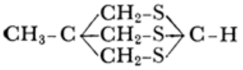
[9] A. Schönberg and L. V. Vagha, *Ber.*, **64**, 2577 (1931).

[10] J. Hine, "Divalent Carbon," Ronald Press, New York (1964).

[11] S. Oae, W. Tagaki and A. Ohno, *Tetrahedron*, **20**, 417, 427, 437 (1964).

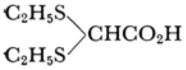
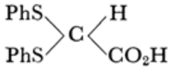
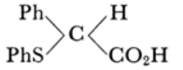
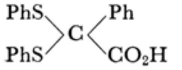
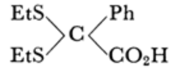
TABLE I. CARBOXYLATION OF SOME SULFIDES IN DIMSYLSODIUM - DIMETHYL SULFOXIDE (ROOM TEMPERATURE, 17 HR.)

$$RH \xrightarrow{CH_3SOCH_2^{\ominus}Na^{\oplus}} [R^{\ominus}] \xrightarrow[2)\ H^{\oplus}]{1)\ CO_2} RCO_2H$$

RH		Color of the reaction mixture	Recovered RH, %	RCO₂H		
				Yield %	M. p., °C	Thermal decomp., °C
$PhCH_2$-S-C_2H_5	(I)	Dark purple	83	trace[a]	—	—
$PhCH(SC_2H_5)_2$	(II)	Dark green-purple	38	31	79—81[b]	>140
$PhCH_2SPh$	(III)	Dark orange-red	35	58	101—101[c]	>270
$PhCH(SPh)_2$	(IV)	Dark orange-red	42	49	140—141[d]	>140
$H_2C(SRh)_2$	(V)	Dark yellow	25	51	104—105[e]	>205
	(VI)	Dark green	85	none	—	—
	(VII)	Dark green	—	none[f]	—	—

a) Not identified. b) Lit., 81°C[13] c) Lit., 101—102°C[14] d) Lit., 143°C[15]
e) Lit., 104—106°C[16] f) Mainly a resinous product

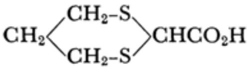
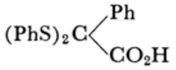
TABLE II. THE AMINE-CATALYZED DECARBOXYLATION OF SOME MERCAPTO-CARBOXYLIC ACIDS IN DIMETHYL SULFOXIDE

Acid		Temp., °C	k_1, sec⁻¹	Rec. rate.
	(VIII)[a]	160	4.85×10^{-5}	1
	(IX)[a]	90	1.95×10^{-4}	2.80×10^{3}
	(X)[a]	90	3.71×10^{-4}	5.33×10^{3}
	(XI)[b]	18.5	3.20×10^{-3}	9.57×10^{7}
	(XII)[b]	80	1.65×10^{-3}	7.47×10^{4}

a) 0.5×10^{-3} mol. of acid and 5×10^{-3} mol. of triethanol amine in 50 ml. D. M. S. O.
b) 1.5×10^{-3} mol. of acid and 1.5×10^{-3} mol. of triethylamine in 29 ml. D. M. S. O.

TABLE III. DECARBOXYLATION PRODUCTS

$$RCO_2H \xrightarrow{\text{in } CH_3SOCH_3} RH + CO_2$$

RCO₂H	Temp., °C	Time hr.	Yield, % of	
			CO₂[a]	RH
$(C_2H_5S)_2CHCO_2H$	150	30	93	90±5[b]
	150	25	97	90±5[b]
	80	10 min.	95	57
$(PhO)_2CHCO_2H$	150	35	100	—[c]

a) Trapped as barium carbonate.
b) Determined by gas chromatography.
c) Unidentified, but the product was shown to contain phenol from the infrared spectra.

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12) E. Baumgarten and C. R. Hauser, *J. Am. Chem. Soc.*, **66**, 1039 (1944).

13) F. Weygand, W. Steglich and H. Janner, *Ann.*, **658**, 128 (1962).

14) Z. J. Vejdelek, O. Nemecek and A. Simek, *Collection Czech, Chem. Commun.*, **28**, 2618 (1963) ; *Chem. Abstr.*, **59**, 15269a (1963).

15) R. Escales and E. Baumann, *Ber.*, **19**, 1787 (1886).

16) R. Otto and J. Troeger, ibid., **25**, 3425 (1892).

connected to an air-tight automatic buret.[12] Sulfide (2.0 g.) was weighed in a glass tube, dissolved in 25 ml. of a dimsylsodium solution which had been transferred from the above automatic buret, and sealed under an air-free nitrogen atmosphere. The reaction mixture was then left at room temperature for 17 hr., after which the tube was opened and the contents poured into an excess suspension of solid carbon dioxide in ether to give a salt suspension. Water was added to the salt suspension, and the water layer was extracted with ether twice. The ether layers were combined, washed with water, dried and concentrated, and the residue was vacuum-distilled to give the unreacted sulfide. The water layer was acidified with hydrochloric acid and then extracted with ether three times. The ether extract was dried and concentrated to give the mercapto acid. The results are shown in Table I. An air-free nitrogen atomsphere is not necessarily required for the purpose of the carboxylation, and the reaction time can be shortened by increasing the reaction temperature to 50°C.

Decarboxylation Reaction.—*Kinetics.*—The carboxylic acid and triethylamine or triethanolamine were dissolved in anhydrous dimethyl sulfoxide and heated in a constant temperature bath under an air-free nitrogen stream. Carbon dioxide was absorbed in dilute solutions of sodium hydroxide and back-titrated with dilute sulfuric acid. While the kinetic procedures will be reported in detail elsewhere, the results are shown in Table II. The relative rates were calculated from the apparent activation energy of the decarboxylation reaction of the acid (X) (29.2 kcal./M) obtained from Arrhenius plot.

The Product Analysis of the Decarboxylation.—In a 100-ml. two-necked flask with a nitrogen gas inlet tube and a reflux condenser there was placed 0.01 mol. of an acid and 50 ml. of dimethyl sulfoxide. The reaction mixture was then heated on an oil bath under the bubbling of air-free nitrogen gas. The carbon dioxide evolved was led through a dry ice-cooled trap to an absorbing trap containing 0.2 M barium hydroxide. The heating was then continued, by replacing the absorbing trap with another one, until the evolution of carbon dioxide was no more observed. The reaction mixture was cooled and analyzed by gas chromatography and finally subjected to a fractional distillation. The results are shown in Table III.