

DISPROPORTIONATION OF SOME BENZYL SULFIDES

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Disproportionation reactions of sulfides induced by strong acids have been reported only for a few aliphatic sulfides^{1,2}. We have observed a rapid disproportionation of benzyl sulfides during the synthesis of 4,4'-diamino-2,6-dimethyl-bis(benzyl)-sulfide (A), a monomer we use³ in preparing linear polyamides amenable to structural determination by cleavage methods. A itself, but not the related (4-carboxybenzyl)-carboxymethyl-sulfide (B)⁴, disproportionates upon treatment with hot concentrated HCl.

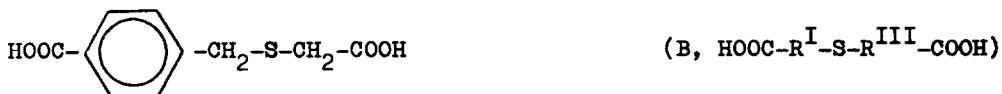
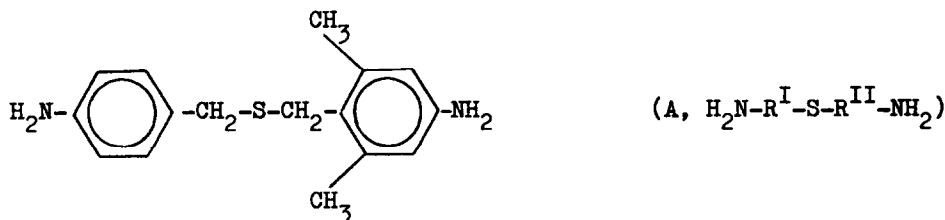


Table 1 summarizes the results obtained on converting different sulfides into A under various conditions. The products were identified by comparing R_f -values, Mass- and NMR-spectra with those of reference samples of A and of the two symmetrical sulfides A_I $\{(\text{H}_2\text{N}-\text{R}^{\text{I}})_2\text{S}\}$ and A_II $\{(\text{H}_2\text{N}-\text{R}^{\text{II}})_2\text{S}\}$. A (M^+ 272, mp 82-4°C after recrystallization from ether/n-hexane) was obtained most conveniently either by relatively mild acid hydrolysis or by basic hydrolysis of the diformyl

Table 1. Composition of the sulfide mixture obtained from compounds of the type $-R^I-S-R^{II}-$ under various conditions

Starting sulfide	Conditions ^a	Composition of the isolated mixture of sulfides ^b :	
		A	A _I + A _{II}
$\begin{array}{l} R^I-NH-COCH_3 \\ \\ S \\ \\ R^{II}-NH-COCH_3 \end{array}$	6N HCl (H ₂ O), reflux, 39hr	38%	62%
	4N H ₂ SO ₄ (H ₂ O/MeOH ^c), 85°C, 2 1/2hr	44%	56%
	1.2N NaHSO ₄ (H ₂ O/MeOH ^c), 85°C, 6hr	70%	30%
	5N KOH (H ₂ O/EtOH ^d), reflux, 7 3/4hr	e	not obsd.
$\begin{array}{l} R^I-NH-COH \\ \\ S \\ \\ R^{II}-NH-COH \end{array}$	0.5N HCl (H ₂ O/MeOH ^c), 30°C, 3 1/2hr	e	not obsd.
	3N KOH (H ₂ O/MeOH ^c), reflux, 1hr	100%	not obsd.
A	6N HCl (H ₂ O), 110°C, 2hr	29%	71%
$\begin{array}{l} R^I-NO_2 \\ \\ S \\ \\ R^{II}-NO_2 \end{array}$	Ru ₃ (CO) ₁₂ (N-methylpyrrolidine), H ₂ /CO (1:1), 200at, 160°C, 6hr	63%	37%

- a) Molar ratios: HCl / HOC-NH-R^I-S-R^{II}-NH-COH = 3; O₂N-R^I-S-R^{II}-NO₂ / Ru₃(CO)₁₂ = 100; in all other cases acid (or base) / starting sulfide = 100.
- b) This mixture represents more than 90% of the sulfides produced. The isolation was performed as follows: If an organic solvent was used for the reaction, this was first evaporated. In the case of the catalytic reduction the mixture was separated on a silica gel column by eluting with different proportions of benzene and acetone. In the other cases the solutions were made basic and the mixture was extracted from the suspension with chloroform and isolated by evaporation of the solvent under reduced pressure.
- c) 3:2 by vol.
- d) 1:3 by vol.
- e) The NMR spectrum indicated that the product was mainly A. The spectrum showed a signal (3.93 ppm in CDCl₃ from TMS) attributable to the OH proton of a benzyl alcohol.

precursor $\text{HCO-NH-R}^{\text{I}}\text{-S-R}^{\text{II}}\text{-NH-COH}$ (mp 198-201°C). A_I $\left\{ \text{M}^+ 244, \text{mp } 104\text{-}5^\circ\text{C (Lit.}^5\right.$
 $105^\circ\text{C)} \left. \right\}$ was prepared according to O. Fischer⁵. A_{II} ($\text{M}^+ 300, \text{mp } 175\text{-}6^\circ\text{C}$) was iso-
 lated from the products of the acid hydrolysis of the diacetyl precursor
 $\text{CH}_3\text{CO-NH-R}^{\text{I}}\text{-S-R}^{\text{II}}\text{-NH-COCH}_3$ (mp 205-6°C). The approximate ($\pm 5\%$) quantitative
 composition of the sulfide mixtures reported in Table 1, is based on NMR-spec-
 tra of solutions in CDCl_3 . These spectra revealed a 2:3 ratio of methylene to
 methyl protons, indicating that A_I and A_{II} , when present in the product, were
 in approximately equimolar amounts. Hence, the composition was calculated using
 the heights of the relatively well separated resonance signals of the methyl
 groups of A and A_{II} (2.20 ppm and 2.27 ppm respectively from TMS).

When A or its diacetyl derivative was treated with hot 6N HCl, 60% to 70% of
 the sulfide mixture obtained consisted of the disproportionation products A_I
 and A_{II} . On the contrary B remained unaltered upon treatment with 6N HCl in H_2O
 at 100°C for 15hr, as indicated by the absence of appreciable changes in mp,
 NMR- and Mass-spectra of the product.

There were no disproportionation reactions observed for treatment with KOH.
 However the basic hydrolysis of $\text{CH}_3\text{CO-NH-R}^{\text{I}}\text{-S-R}^{\text{II}}\text{-NH-COCH}_3$ and the acid hydroly-
 sis under mild conditions of $\text{HCO-NH-R}^{\text{I}}\text{-S-R}^{\text{II}}\text{-NH-COH}$ indicated in Table 1 were
 accompanied by some cleavage of the C-S bonds. A cleavage of the C-S bonds un-
 der basic conditions was observed¹ also when methyl β -methylthiopropionate
 was treated with 2N NaOH.

It seems fairly certain^{2,6} that the disproportionation of an unsymmetrical sul-
 fide induced by a strong acid involves as the primary step the coordination of
 a proton by the unshared electrons of the sulfur atom. Disproportionation then
 takes place as a consequence of the equilibrium which is established between
 the protonated sulfide and its dissociation products, thiol and carbonium ion[§].
 A reason for the stability of B to hot 6N HCl might be that the two electrophilic
 carboxyl groups decrease the electron availability on the sulfur atom, pre-
 venting protonation at this site. A similar explanation has been proposed¹ for
 the stability of methylthio- and ethylthio-acetic acid to 6N-acid and seems to
 be in accordance with the observed⁷ stability of phenyl-carboxymethyl-sulfide
 towards AlBr_3 in chlorobenzene. Alternatively one might suppose that in B only
 one type of C-S bond (probably the benzyl to sulfur bond) is overwhelmingly in-
 volved in the above equilibrium because of the high energy of the carbonium
 ion deriving from the cleavage of the other type of C-S bond.

§ Challenger and Hollingworth¹ have proposed another mechanism whereby protona-
 ted and nonprotonated sulfide interact first to give thiol and sulfonium ion,
 the latter decomposing to carbonium ion and sulfide.

Disproportionation was observed also in the catalytic reduction^{8,9} of $O_2N-R^I-S-R^{II}-NO_2$ (mp 127-8°C) with $Ru_3(CO)_{12}$ as the catalyst in basic medium (Table 1). In this case the disproportionation may have been induced by the transition metal atom forming a coordination complex with the sulfur¹⁰.

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