Anal. Calcd. for $C_{14}H_8N_6OS_2$: C, 51.84; H, 2.49; N, 25.92; S, 9.89. Found: C, 51.80; H, 2.43; N, 26.35; S, 10.29.

3-Chloro-1,2,4-benzotriazine. A suspension consisting of 1.00 g. of 3-chloro-1,2,4-benzotriazine-1-oxide, 0.40 g. of zinc dust, and 0.30 g. of ammonium chloride in 25 ml. of water was stirred mechanically for 17 hr. at room temperature. The reaction mixture was diluted with an equal volume of acetic acid and then filtered. The filtrate was extracted with hexane and the combined hexane extracts were washed with water, dried over sodium sulfate, and evaporated to dryness *in vacuo*. Crystallization of the residue from pentane yielded 0.35 g. of 3-chloro-1,2,4-benzotriazine, m.p. 96–98°.

3-Hydrazino-1,2,4-benzotriazine. Treatment of 1.0 g. of 3-chloro-1,2,4-benzotriazine with 0.5 gm. of hydrazine hydrate with warming gave immediately a dark yellow solution which on standing crystallized. The solid was taken up in 35 ml. of ethanol and allowed to crystallize. The crystals were collected and recrystallized from benzene to give 3-hydrazino-1,2,4-benzotriazine, yield 0.55 g., m.p. 173–175°.

3-(β-Dimethylaminoethyl)amino-1,2,4-benzotriazine. A suspension of 1.0 g. of 3-(β-dimethylaminoethyl)amino-1,2,4-benzotriazine-1-oxide, 0.4 g. of zinc dust, and 0.3 g. of ammonium chloride in 25 ml. of water was stirred mechanically for 17 hr. at room temperature. The reaction mixture was diluted with water and extracted with chloroform and benzene. The combined chloroform and benzene extracts were washed with water, dried over sodium sulfate, and evaporated to dryness *in vacuo*. The residue was taken up in hexane and allowed to crystallize giving 0.57 g. of 3-(β-dimethylaminoethyl)amino-1,2,4-benzotriazine, m.p. 98–100°.

CHICAGO 80, ILL.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, ST. OLAF COLLEGE]

Reactions of Diamines with Isocyanates and Isothiocyanates

OLIVER STOUTLAND, LON HELGEN, AND COURTLAND L. AGRE[1]

Received January 9, 1959

Diamines react with less than equivalent quantities of isocyanates and isothiocyanates to yield the mono- and disubstituted ethylenediamines and recovered diamine. The distribution of products is dependent on the reactivity of the reagent, on concentration, and on the solvent.

Recently it was shown[2] that acids react with diamines to give amides and recovered diamine in nearly the predicted yields based on random distribution. It was of interest to observe if the more facile reactions of diamines with isothiocyanates and isocyanates might yield similar distributions of products.

Amines react with isocyanates to give substituted ureas.[3] Similarly, reaction of diamines with equivalent amounts of isocyanates would be expected to give addition at each of the two amino groups. With less than two moles of isocyanates, the diamines should give mixtures in which the relative yields of the products would depend on the ratios of reactants.

$$H_2N(CH_2)_xNH_2 + b\ RNCO \longrightarrow \underset{(I)}{H_2N(CH_2)_xNH_2} + \underset{(II)}{RNHCONH(CH_2)_xNH_2} + \underset{(III)}{RNHCONH(CH_2)_xNHCONHR}$$

There is the possibility that II would react with a second molecule of isocyanate to give $(RNHCO)_2N(CH_2)_xNH_2$ (IV), but the decreased basicity of the substituted nitrogen in II relative to the primary amine should minimize this reaction.

In the above equation, when b is greater than O but less than 2, the recovery of I would be $\left(\frac{2-b}{2}\right)^2$, the formation of III would be $\left(\frac{b}{2}\right)^2$, and the yield of II would be $\left(b - \frac{b^2}{2}\right)$. When the reactants are present in equimolar quantities and b therefore is 1, the respective yields of I, II, and III would be 25%, 50%, and 25%.

The reaction of amines with isocyanates is known to occur very rapidly. It thus would be anticipated, as frequently was encountered, that the yield of III might be above the expected value due to a concentration effect at the instant of mixing the reactants. It is known[3] that isocyanates vary appreciably in their reactivities depending on the nature of the alkyl or aryl groups. It would be reasonable to expect that the isocyanates with the lesser reactivity would approach the statistical distribution more closely. The reactions of diamines with isothiocyanates[4] would parallel these considerations and substituted thioureas would result. The lower reactivity of the isothiocyanates would cause slower reactions and thus allow an approach to the statistical distribution.

Ideally, in each run the three products, I, II and III, would be isolated quantitatively. However, once the existence of all three products was established, it was expeditious to isolate only the disubstituted product III quantitatively and on occasion product II. The separation was accomplished due to the low solubility of the disubstituted compound in dilute acid solution in contrast to the appreciable solubility of the other products.

The data presented in Table I relate to the yields

---

[1] To whom requests for reprints should be addressed.

[2] C. Agre, G. Dinga, and R. Pflaum, *J. Org. Chem.*, **21**, 561 (1956).

[3] J. Saunders and R. Slocombe, *Chem. Rev.*, **43**, 203 (1948).

[4] D. Schroeder, *Chem. Rev.*, **55**, 181 (1955).

TABLE I

DISUBSTITUTED PRODUCTS III[a] FROM ETHYLENEDIAMINE AND RNCS OR RNCO

RNCS	Solvent	Value "b"[b]	Per Cent III[c]	M.P.,[d] °C.	Recryst. Solvent	Formula	N Analysis Calcd.	N Analysis Found
Ethyl	Isopropyl alcohol	1.0	88	127–128	Ethanol	$C_8H_{18}N_4S_2$	23.9	23.8
Allyl	Isopropyl alcohol	1.0	87	98–99	Ethanol	$C_{10}H_{18}N_4S_2$	21.7	21.4
n-Butyl	Isopropyl alcohol	1.0	88	137–138	Ethanol	$C_{12}H_{26}N_4S_2$	19.3	19.3
n-Heptyl	Isopropyl alcohol	1.0	83	134–135	Ethanol	$C_{18}H_{38}N_4S_2$	15.0	15.1
Phenyl	Isopropyl alcohol	1.0	99	195–196	Acetic acid	$C_{16}H_{18}N_4S_2$	17.0	17.2
Phenyl	Water	1.0	164					
Phenyl	Benzene	1.0	11					
Phenyl	Ether	1.0	17					
Phenyl	Chloroform	1.0	54					
Phenyl	Xylene	0.5	15					
RNCO								
o-Nitrophenyl	Isopropyl alcohol	1.0	176	256–258	Acetic acid	$C_{16}H_{16}N_6O_6$	21.6	21.1
2,5-Dichlorophenyl	Isopropyl alcohol	1.0	154	295–299	Dimethylformamide	$C_{16}H_{14}Cl_4N_4O_2$	12.8	13.1
α-Naphthyl	Isopropyl alcohol	1.0	166	282–284	Dimethylformamide	$C_{24}H_{22}N_4O_2$	14.1	14.3
m-Chlorophenyl	Isopropyl alcohol	1.0	151	261–263	Acetic acid	$C_{16}H_{16}Cl_2N_4O_2$	15.3	15.2
o-Tolyl	Isopropyl alcohol	1.0	125	250–252	Acetic acid	$C_{18}H_{22}N_4O_2$	17.1	17.3
Octadecyl	Chloroform	0.9	104	185–186	Acetic acid	$C_{40}H_{82}N_4O_2$	8.6	8.6
Phenyl	Isopropyl alcohol	1.0	128	247–248[e]	Acetic acid	$C_{16}H_{18}N_4O_2$	18.8	18.7
Phenyl	Isopropyl alcohol	0.4	230					
Phenyl	Benzene	1.0	107					
Phenyl	Chloroform	1.0	135					

[a] Disubstituted products $RNHCONHCH_2CH_2NHCONHR$ or $RNHCSNHCH_2CH_2NHCSNHR$. [b] Ratio of moles of RNCS or RNCO to moles of ethylenediamine. [c] Based on yield expected from random distribution. [d] All melting points are uncorrected. [e] Recorded melting points: 263,[5] 245,[6] 298[7].

of disubstituted products III obtained from ethylenediamine. The isocyanates, in practically every instance, gave relatively high yields of III, due probably to a concentration effect. In contrast to this, products from the isothiocyanates were formed in some instances in approximately the expected yields. There is an appreciable solvent effect, which we shall not now try to explain, as shown by some of the reactions involving phenyl isothiocyanate in which the yield of III is much lower than expected. It is evident that a solvent like benzene can be used to good advantage in the preparation of high yields of monosubstituted compounds (II), since the formation of III is very low. This solvent effect appears less significant with the isocyanates.

Similar results were encountered in the data of Table II, which represent the yields of III when the diamine was hexamethylenediamine. Concentration effect again apparently was responsible for the high yield of III from isocyanates. Throughout this research III was obtained in unusually high yield when "*b*" was appreciably below unity, especially with the isocyanates.

In a number of instances the monosubstituted products II were isolated and characterized, as shown in Table III. Except in the systems where the alkyl groups were relatively short aliphatic chains, these products were solids. These monosubstituted products from ethylenediamine decompose slightly above their melting points.

Titration of aliquot portions of the reaction mixtures showed active amine in quantity equal to the total equivalents of original amine minus the iso(thio)cyanates employed. A portion of this amine in each instance was accounted for by the product II. The balance ought to be unreacted diamine. In a number of instances this excess diamine, at least in part, was isolated and identified. However, the recovery of I and II were seldom attempted quantitatively.

EXPERIMENTAL

The following example is a typical illustration of the procedure employed in this study.

Addition of phenyl isothiocyanate to ethylenediamine. A solution of 27 g. (0.20 mole) of phenyl isothiocyanate in 50 ml. of absolute ether was added dropwise to a vigorously stirred solution of 12 g. (0.20 mole) of anhydrous ethylenediamine in 300 ml. of isopropyl alcohol. Addition required 40 min., during which period the temperature rose slightly and a white precipitate separated. The mixture was stirred for 2 hr., was diluted with water to about 800 ml., and was allowed to stand overnight. Titration of a portion of the clear solution with aqueous hydrochloric acid (methyl orange) indicated a residual free amine content equivalent to 5.9 g., or 49% of the original diamine.

The solution was poured into a Pyrex baking dish, 18 ml. concd. hydrochloric acid was added, and evaporation to dryness was effected on a steam bath. The white residue was suspended in 250 ml. of water at about 50° and was stirred to dissolve all soluble material. The remaining solid was removed by filtration and was washed with warm water. The *N,N'*-bisphenylthiocarbamylethylenediamine weighed 13.7 g., equivalent to 21% of the original diamine. Recrystallization was effected from acetic acid, m.p. 195–196°.

Anal. Calcd. for $C_{16}H_{18}N_4S_2$: N, 17.0. Found: N, 17.2.

The aqueous filtrate was cooled and then made very basic

TABLE II[a]

DISUBSTITUTED PRODUCTS III FROM HEXAMETHYLENEDIAMINE AND RNCS OR RNCO

RNCS	Solvent	Value "b"	Per Cent III	M.P., °C.	Recryst. Solvent	Formula	N Analysis Calcd.	N Analysis Found
Ethyl	Isopropyl alcohol	1.0	102	102–103	Ethanol	$C_{12}H_{26}N_4S_2$	19.3	19.2
Allyl	Isopropyl alcohol	1.0	107	103–104	Ethanol	$C_{14}H_{26}N_4S_2$	17.8	17.8
n-Heptyl	Isopropyl alcohol	1.0	98	112–113	Ethanol	$C_{22}H_{46}N_4S_2$	13.0	12.9
Phenyl	Isopropyl alcohol	1.0	95	145–147	Ethanol	$C_{20}H_{26}N_4S_2$	14.5	14.5
Phenyl	Chloroform	1.0	98					
Phenyl	Chloroform	0.5	103					
RNCO								
m-Chlorophenyl	Isopropyl alcohol	1.0	154	188–190	Ethanol	$C_{20}H_{24}Cl_2N_4O_2$	13.2	13.4
α-Naphthyl	Isopropyl alcohol	1.0	155	248–251	Acetic acid	$C_{28}H_{30}N_4O_2$	12.4	12.4
o-Tolyl	Isopropyl alcohol	1.0	126	229–231	Acetic acid	$C_{22}H_{30}N_4O_2$	14.7	14.7
Phenyl	Isopropyl alcohol	1.0	148	219–221	Ethanol	$C_{20}H_{26}N_4O_2$	15.8	15.7
Phenyl	Chloroform	1.0	186					
Phenyl	Chloroform	0.5	330					

[a] Same interpretations as in Table I.

TABLE III

MONOSUBSTITUTION PRODUCTS II[a] AND DERIVATIVES

Material	M.P., °C.	Solvent	Formula	Neutral Equiv. Calcd.	Neutral Equiv. Found	Nitrogen Calcd.	Nitrogen Found
N-Phenylthiocarbamylethylenediamine	135–136	Chloroform	$C_9H_{13}N_3S$	195	196	...	...
N'-C_6H_5NCO derivative	185–187	Acetic acid	$C_{16}H_{18}N_4OS$	...	...	17.8	18.2
N'-Benzoyl derivative	150–152[b]	Acetone					
N-Phenylcarbamylethylenediamine	115–116	Chloroform	$C_9H_{13}N_3O$	179	182	23.3	22.8
N'-Benzoyl derivative	214–215[c]	Acetone	$C_{16}H_{17}N_3O_2$	...	...	14.8	14.8
N'-C_6H_5NCS derivative	185–186						
N-Phenylthiocarbamylhexamethylenediamine	89–92		$C_{13}H_{21}N_3S$	251	251	...	...
N'-C_6H_6 NCO derivative	132–133	Ethanol	$C_{20}H_{26}N_4OS$	...	...	15.1	15.1
N-Phenylcarbamylhexamethylenediamine	114–117		$C_{13}H_{21}N_3O$	...	...	17.8	17.5
N'-C_6H_5NCS derivative	132–134						

[a] II represents $C_6H_5NHCONH(CH_2)_xNH_2$ or $C_6H_5NHCSNH(CH_2)_xNH_2$. [b] Reported[8] m.p. 150°. [c] Reported[8] m.p. 215°.

with concentrated sodium hydroxide solution. There separated an abundant yield (20.3 g., or 104% based on random distribution) of the monosubstituted product, phenylthiocarbamylethylenediamine. This was recrystallized from water, m.p. 136–137°. The neutral equivalent was determined by titration with aqueous hydrochloric acid (methyl orange).

Anal. Calcd. for $C_9H_{13}N_3S$: neut. equiv., 195. Found: neut. equiv., 196.

The filtrate from the above product was distilled to dryness to recover the diamine. The distillate was acidified with hydrochloric acid and was evaporated to dryness to leave 3.5 g. of the salt. Treatment with benzoyl chloride in aqueous alkali gave the known dibenzylethylenediamine.

Acknowledgement. We are indebted to the Research Corporation for a grant which allowed the conduct of this research. The study was first undertaken under a grant provided by the Dearborn Chemical Corp., to whom thanks also are expressed.

NORTHFIELD, MINN.

---

(5) Beilstein XII, page 365, Fourth Edition.

(6) Curtius and Hectenberg, *J. prakt. Chem.*, **105**, 289 (1923).

(7) von Alphen, *Rec. trav. chim.*, **54**, 595 (1935).

(8) A. Hill and S. Aspinall, *J. Am. Chem. Soc.*, **61**, 822 (1939).