

values 1.3,¹² 15.6,¹³ 22.9¹⁴ and 24.5¹⁵ E. U. per gram atom, respectively, for carbon, hydrogen, nitrogen and oxygen.

In view of the accuracy of the measurements involved, we feel that the uncertainty in the $T\Delta S$ term cannot in any case exceed ≈ 300 calories. The accuracy with which the heats of combustion of carbon and hydrogen are now known should preclude any great uncertainty due to their use even in the largest molecules considered. Consequently we feel that the accuracy of the free energy values is limited largely by the accuracy of the combustion data. A study of these values where more than one worker has burned the compound will show differences from 2000 to 4000 calories per mole.

Summary

1. The heat capacities of seven nitrogen-containing organic compounds have been measured over the temperature range 90 to 298°K.
2. The entropies of these seven compounds have been calculated from the heat capacity data.
3. The free energies of these compounds have been calculated and their accuracy was found to have been limited largely by the accuracy of the combustion data.

¹² Lewis and Gibson, *THIS JOURNAL*, **39**, 2581 (1917).

¹³ Giaque, *ibid.*, **52**, 4816 (1930).

¹⁴ Giaque, private communication.

¹⁵ Giaque and Johnston, *THIS JOURNAL*, **51**, 2300 (1929).

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF WASHINGTON]

DESULFURIZATION OF THIOUREAS BY BROMATE AND IODATE SOLUTIONS

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In preparing thioureas for the purpose of studying desulfurization effects on them by bromate and iodate solutions, it was observed that certain bases, though closely related, either do or do not react with phenyl mustard oil or with thiocyanic acid to yield the corresponding thioureas. For example, while *m*-nitroaniline¹ easily yields phenyl-*m*-nitrophenylthiourea, the corresponding thioureas could not be formed with ortho- or with para-nitroaniline, either by direct heating or in solvents. By direct heating the *p*-nitroaniline, however, gave thiocarbanilide and di-*p*-nitrophenylthiourea²

¹ Brückner, *Ber.*, **7**, 1235 (1874); Losanitsch, *ibid.*, **14**, 2365 (1881); Kjellin, *ibid.*, **36**, 197 (1903).

² For similar product formed by heating 3-nitrothiocarbanilide, see Elbs and Schlemmer, *J. prakt. Chem.*, [2] **27**, 480 (1883).

but no mono-*p*-nitrothiocarbaniide. Also 3-nitro-*o*-toluidine, which differs but little from *m*-nitroaniline, gave no thiourea.

Furthermore, while phenyl mustard oil and phenyl isocyanate react exothermically with piperidine to give phenylpiperidylthiourea³ and phenylpiperidylurea, piperidine thiocyanate could not be isomerized to piperidylthiourea, even when heated at 220°. This is remarkable in view of the fact that piperidine cyanate easily yields piperidylurea.⁴ The play of affinity in these and other cases is very selective⁵ and theories of steric hindrance, relative alkalinities, etc., are inapplicable to account for these negative results.

Frequently with unsymmetrical thioureas and less often with unsymmetrical ureas, it was observed both in the literature and in experiments that the melting points are variable, depending upon the solvent used, upon the thermal conditions involved in their preparation, and upon the method of making the melting point determinations. This variability was especially observed by Kjellin, who showed that two molecules of the unsymmetrical thiourea frequently undergo intermolecular double decomposition⁶ so as to yield two different symmetrical thioureas



TABLE I
MELTING POINTS OF THIOUREAS

X of Ph-NH-CS-NHX	Lit. m. p.	1st m. p.	2d m. p.	3d m. p.	4th m. p.	5th m. p.	Oil in m. p. tube
<i>p</i> -Bromophenyl	158	167	154	150	148	148	+
<i>p</i> -Chlorophenyl	152	158	155	153	153		+
2,5-Dichlorophenyl		168	154	140	130	125	+
2,4-Dichlorophenyl	157	168	130	120			+
<i>p</i> -Tolyl	142	172	140	160	160		-
<i>p</i> -Ethoxy	129	144	122	122	124	122	+
2,4-Dimethylphenyl	125.5	133	Did not resolidify				
	126	134					
4-Hydroxy-2-methylphenyl		177	Did not resolidify				
β -Naphthyl	157	167	169	167	165	164	+
2-Hydroxy-4-methylphenyl	110	117	112	102	Did not resolidify		-

³ Gebhardt, *Ber.*, **17**, 3040 (1884).

⁴ Cahours, *Ann. chim.*, [3] **38**, 84 (1853).

⁵ Aminization of ortho and para but not meta of chloro, bromo, hydroxy or alkyloxy nitrobenzenes and the easy hydrolysis of ortho and para but not the meta nitroanilines are examples of selective affinities that are converse to the above thioureas. Because the hydrochloride of *m*-nitroaniline is less easily hydrolyzed than the hydrochloride of the ortho and para nitroanilines, and the hydrochloride of piperidine is the least hydrolyzed, and it is apparent that relative alkalinities are not involved.

⁶ Elbs and Schlemmer, *Ber.*, **36**, 194 (1903), give another type of decomposition: $2\text{RNHCSNHR}' \longrightarrow \text{RNCS} + \text{R}'\text{NCS} + \text{R}'\text{NH}_2 + \text{RNH}_2$, whose products can unite to form the two symmetrical thioureas. The fact that thioureas isomerize more readily than ureas and these decompose in accordance with this reaction, accounts for the greater thermal sensitiveness of the thiourea over that of the ureas.

TABLE II
 MELTING POINT OF UREAS

X of Ph-NH-CO-NHX	MELTING POINT OF UREAS						
	Lit. m. p.	1st m. p.	2d m. p.	3d m. p.	4th m. p.	5th m. p.	Oil in m. p. tube
2,5-Dichlorophenyl		200.5		200	201		
2,4-Dichlorophenyl		206.5	206				
<i>p</i> -Tolyl	213-231	212	208	204	205	203	—
<i>o</i> -Tolyl	196	196	196	196	196	196	—
Methyl	150	151	150	150		151	—
Allyl	113	111	108	117	119	107	
	115.5	117	117	107	116	107	—

In the tables are given data of successive melting points on the same samples in the same capillary tube.

Though it has long been known⁷ that alcohol unites with mustard oils to yield thiocarbanilic esters, it has been most commonly used as the solvent in the preparation of thioureas from phenyl mustard oil and bases. This alcohol often accounts for the variability of products. We have employed cold toluene solutions as the most successful condition for the preparation of thioureas.⁸

It was found that certain thioureas are smoothly desulfurized by iodate solution. For example, all thioureas of the types RNHCSNH₂ and RNHCSNHR' except phenylbenzylthiourea were thus desulfurized, but thioureas of types RR'NCSNH₂ and R₂NCSNHR and R₂NCSNR₂ were entirely negative. It was found that bromate was as effective as iodates, in alkaline solutions, for the purpose of such desulfurization and that with either desulfurizations are smoother than with lead, mercury or silver compounds, since heating alone yields either the cyanamide or the urea which can be filtered off and crystallized from organic solvent so as to obtain pure and substantially quantitative yields. The progress of desulfurization can easily be followed by the lead test. Whereas thiocarbanilide is desulfurized in a few minutes, some of the thioureas required many hours of heating before the product gave no test for sulfur.

The thioureas, the bromate or the iodate, and sodium hydroxide in equal weights were heated⁹ in sufficient water for such time as was necessary to give negative tests with lead solution. The precipitate was filtered off, washed with water and finally recrystallized from toluene or other solvent. With thioureas of the type RNHCSNH₂, forming, of course, the cyanamide,

⁷ Hofmann, *Ber.*, **2**, 74 (1869); **3**, 772 (1870); Bamberger, *ibid.*, **15**, 2164 (1882); Fromm, *ibid.*, **42**, 1957 (1909).

⁸ Since thiocyanic acid does not blacken when heated with alkaline lead solutions, and thioureas do, it is useful in checking the formation of such thioureas.

⁹ In preparing the ureas from the thioureas, a decomposition into base and thiocyanate took place to some extent, the former being detected by odor and the latter by ferric solutions. Neither phenyl mustard oil nor the original thiourea give the red color with ferric solution; *o*-tolylcyanamide gives a red color upon heating; this disappears upon cooling.

TABLE III

NEW THIOUREAS						
R' of	M. p., °C.	Crystal form	Nitrogen, %		Sulfur, %	
			Calcd.	Found	Calcd.	Found
Type C ₆ H ₅ NHCSNHR'						
2,5-Dichlorophenyl	168	Needles	9.43	9.32		
<i>o</i> -Phenetidyl	145	Prisms	10.29	10.46		
4-Hydroxy-2-methylphenyl	177	Prisms			12.40	12.78
2,4-Dichlorophenyl	168	Prisms	10.00	10.62		
Type H ₂ NCSNHR'						
<i>p</i> -Methoxyphenyl	210	Prisms			17.58	17.62
2,5-Dichlorophenyl	185	Prisms	32.10	31.94	14.49	14.52
Type R'NHCSNHR						
2,4-Xylyl- <i>o</i> -tolyl	162	Needles			11.85	11.88

TABLE IV

NEW UREAS FROM THIOUREAS					
Thiourea	Desulfurizing reagent	M. p., °C.	Crystal form	Calcd.	Found
Phenyl-2,4-dichlorophenyl	KBrO ₃	208	Prisms	Cl, 25.24	Cl, 24.93
Phenyl-2-4-dimethylphenyl	KIO ₃	226	Tablets	N, 12.06	N, 11.67
<i>o</i> -Tolyl- <i>p</i> -chlorophenyl	NaBrO ₃	212	Prisms	Cl, 13.61	Cl, 13.82

TABLE V

KNOWN UREAS FROM KNOWN THIOUREAS				
X of PhNH-CS-NHX	Lit. m. p.	M. p., °C.	Crystal form	Desulfurizing reagent
<i>p</i> -Bromophenyl		238	Plates	KIO ₃
<i>p</i> -Chlorophenyl		238		KIO ₃
<i>p</i> -Ethoxyphenyl	161-162	162-185		KBrO ₃
2,4-Dimethylphenyl		226	Tablets	
<i>p</i> -Tolyl		212		KBrO ₃
β -Naphthyl		220-221	Prisms	KIO ₃
<i>o</i> -Tolyl		195		KIO ₃
		196	Needles	KBrO ₃
Phenyl-		237	Needles	KBrO ₃
HOC ₂ H ₄ -		122-123	Plates	KIO ₃
<i>o</i> -Ethylloxyphenyl		175		KIO ₃
Allyl		117		KBrO ₃
Methyl		151		KBrO ₃
(<i>m</i> -NO ₂ C ₆ H ₄ NH) ₂ CS	233	238		KBrO ₃

TABLE VI

KNOWN CYANAMIDES FROM KNOWN THIOUREAS				
X of XNHCSNH ₂	Desulfurizing reagent	M. p., °C., lit.	M. p., °C., found	Crystal form
2,4-Dimethylphenyl	NaBrO ₃	109-110	117	
<i>o</i> -Tolyl	NaBrO ₃	77	76.5	
β -Naphthyl	NaBrO ₃	102	104-106	Plates
α -Naphthyl	NaBrO ₃	135	126	Plates
<i>p</i> -Bromophenyl	NaBrO ₃	112	112	Needles

after filtering, the alkali solutions were acidified with acetic acid, when the cyanamide separated either as an oil or as a solid.

Summary

Bromate in alkaline solution is an efficient reagent for desulfurization of thioureas. Owing to decomposition by heat thioureas often give varied melting points; they are best recrystallized from toluene.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, CASE SCHOOL OF APPLIED SCIENCE]

QUINAZOLINES. IV. ALCOHOLYSIS IN THE QUINAZOLINE SERIES AND THE PREPARATION OF SOME MIXED DIETHERS OF QUINAZOLINE

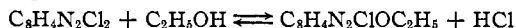
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In the course of some experiments with 2,4-dichloroquinazoline it was observed that one of the two chlorine atoms present in this compound undergoes substitution more readily than the other, and that under proper conditions monochloroquinazolines only are formed. By converting these monochloro derivatives into known compounds, the location of the entering groups was ascertained and the more reactive chlorine atom assigned to the 4-position.¹

When warm alcoholic solutions of 2,4-dichloroquinazoline are treated with potassium cyanide or other salts of weak acids, 2-chloro-4-ethoxyquinazoline is formed. In order to explain this it was assumed that in such solutions of 2,4-dichloroquinazoline there exists an equilibrium between the chlorine at the 4-position and the solvent, thus



and that with conditions providing for the speedy removal of the hydrogen chloride formed, as does the presence of salts of weak acids, the reaction to the right is favored.² This mechanism is not limited to the alcohols, however, for on merely shaking 2,4-dichloroquinazoline with aqueous sodium hydroxide, 2-chloro-4-ketodihydroquinazoline results.³

The formation of 2,4-diethoxyquinazoline (V) from 2-chloro-4-ethoxyquinazoline (I) and alcoholic sodium ethylate was described in an earlier paper.⁴ This and the corresponding reaction between 2-chloro-4-methoxyquinazoline (IV) and methyl alcoholic sodium methylate to give 2,4-dimethoxyquinazoline (II) indicated that mixed diethers of the types III and VI might be prepared by treating 2-chloro-4-ethoxy- and 2-chloro-4-

¹ Lange, Roush and Asbeck, *THIS JOURNAL*, **52**, 3696 (1930).

² Lange and Sheibley, *ibid.*, **53**, 3867 (1931).

³ British Patent 287,179.

⁴ *THIS JOURNAL*, **52**, 3700 (1930).