[Contribution from the Chemical Laboratory of Tufts College]

THE ACTION OF BUTYLMAGNESIUM BROMIDE ON THE AROMATIC ISOTHIOCYANATES

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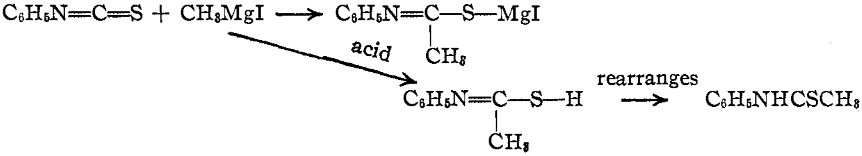
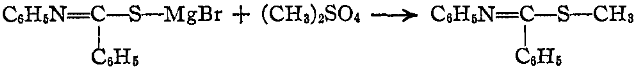
The Grignard reagent reacts with isothiocyanates, the so-called mustard oils, forming thio-amides.[1] In fact, this method is the easiest and most convenient for the preparation of these interesting substances. Accordingly, it has seemed worth while to investigate further this reaction which has been little studied. In this communication the action of the Grignard reagent prepared from *n*-butyl bromide, formerly a rare substance but now obtainable in quantity at a moderate price, on a number of typical isothiocyanates is described.

The reaction with phenyl mustard oil and methylmagnesium iodide is represented by Sachs and Loevy as follows.



$$C_6H_5N{=}C{=}S + CH_3MgI \longrightarrow C_6H_5N{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}S{-}MgI \xrightarrow{\text{acid}} C_6H_5N{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}S{-}H \xrightarrow{\text{rearranges}} C_6H_5NHCSCH_3$$

This assumption of the mechanism of the reaction has since been verified by Gilman[2] who by alkylation of the intermediate addition product showed that the Grignard reagent added to the thiocarbonyl group of the isothiocyanate. The complex resulting from the action of phenylmagnesium bromide on phenylisothiocyanate was used.



$$C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}S{-}MgBr + (CH_3)_2SO_4 \longrightarrow C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}S{-}CH_3$$

Substituted thio-amides of valeric acid, $CH_3CH_2CH_2CH_2CSNHR$, were obtained eventually with butylmagnesium bromide. A crystalline addition product separated from the ether solution on mixing *p*-tolylisothiocyanate with butylmagnesium bromide, but in all other cases except with *p*-phenylene-di-isothiocyanate no such separation was observed. In all cases a large excess of butylmagnesium bromide, usually 50%, was employed. This excess has no apparent effect on the addition complex from the thio-amide. It was possible in this way to drive the reaction more completely in the desired direction, also to avoid losses due to the action of small amounts of moisture, carbon dioxide, etc., on the butylmagnesium bromide and losses due to the incompleteness of the action of magnesium on butyl bromide. The reaction was found in all cases to go very readily with evolution of considerable heat and

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[1] Sachs and Loevy, *Ber.*, **36**, 585 (1903); **37**, 874 (1904).

[2] Gilman, This Journal, **46**, 493 (1924).

apparently was completed in a few minutes. Long standing of the mixture was found to be inadvisable. The yields were especially good with *p*-tolyl- and β-naphthylisothiocyanates, over 90% of those calculated on the basis of the mustard oil.

Experimental Part

Thiovalero-*p*-toluide, $C_4H_9CSNHC_6H_4CH_3$.—Thirty-five g. of butyl bromide was added to 300 cc. of ether containing 6.3 g. of magnesium and a trace of iodine. After the reaction had subsided but while the mixture was still warm, 25 g. of *p*-tolylisothiocyanate was added, a few grams at a time. Sufficient heat was evolved to cause vigorous boiling of the ether solution. A bulky precipitate of ball-like aggregates of white crystals separated from the mixture on standing overnight. This addition product was filtered off by suction, washed with ether and added to dil. hydrochloric acid containing ice, during mechanical stirring. The resulting crystalline product was filtered off and washed with water containing alcohol; yield, 36.5 g. As the anise-like odor of *p*-tolylisothiocyanate was still perceptible the crude substance was recrystallized from alcohol.

Anal. Calcd. for $C_{12}H_{17}NS$: S, 15.4. Found: 15.8.

The toluide is very soluble in ether, benzene or chloroform. It is readily soluble in hot alcohol, separating as the solution cools in slender, lustrous, white needles; m. p., 69–70°. It has an intensely bitter taste and is much less sensitive toward moisture than the corresponding phenyl derivative. No apparent change took place on standing for several months.

Thiovalerotoluide does not dissolve readily or completely in 10% sodium hydroxide solution. The alkaline solution of this substance is unchanged by short heating, for the original substance may be precipitated by the addition of an excess of acid. Longer heating rapidly induces hydrolysis and on neutralization with hydrochloric acid the characteristic odors of valeric acid and hydrogen sulfide developed. It is more quickly attacked by acid, as heating with concd. hydrochloric acid causes an immediate evolution of hydrogen sulfide.

Action of Hydroxylamine.—Five g. of thiovalerotoluide was mixed with an excess of free hydroxylamine in alcohol and the mixture allowed to stand at room temperature

Table I

Thio-amides of Valeric Acid

				Anal. for S, %	
Thiovalero-	Formula	Cryst. form	M. p., ° C.	Calcd.	Found
Anilide	$C_{11}H_{15}NS$	Plates[a]	38–39	16.6	16.8
p-Toluide	$C_{12}H_{17}NS$	Needles	69–70	15.4	15.8
p-Aniside	$C_{12}H_{17}ONS$[b]	Needles	62–63	..	..
p-Chloro-anilide	$C_{11}H_{14}NSCl$	Needles	101.5–102	15.5[c]	14.9[c]
p-Bromo-anilide	$C_{11}H_{14}NSBr$	Flat needles	112	29.4[d]	29.0[d]
Biphenylamide	$C_{17}H_{19}NS$	Tiny needles[e]	147–148	11.8	11.2
β-Naphthylamide	$C_{15}H_{17}NS$	Plates	79–80	13.1	12.8
bis-Thiovalero-*p*-phenylene-diamide	$C_{16}H_{24}N_2S_2$	Plates[f]	198–199	20.8	20.1

[a] Recrystallized from alcohol and water.

[b] Exploded when heated with nitric acid.

[c] Analyzed for chlorine.

[d] Analyzed for bromine.

[e] Poor yield because of tar formation.

[f] Lacks bitter taste because of insolubility.

for several days. Hydrogen sulfide was set free and some ammonia. The precipitate that formed was recrystallized from hot alcohol, separating as feathery needles; m. p., 83–84°. The crude oxime contained a small amount of yellow material which proved to be sulfur, presumably from the action of hydroxylamine on hydrogen sulfide.

$$NH_2OH + H_2S = NH_3 + H_2O + S$$

A similar procedure was followed in the preparation of the other thio-amides except that smaller amounts of isothiocyanates, usually 5–10 g., were used. The ether was removed by spontaneous evaporation, after addition of acid during stirring, in case the addition product could not be separated by filtration.

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Summary

It has been shown that butylmagnesium bromide reacts readily and smoothly with aromatic isothiocyanates, forming substituted thio-amides of valeric acid.

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[CONTRIBUTION FROM THE SCHOOL OF ENGINEERING RESEARCH OF THE UNIVERSITY OF TORONTO]

AN INVESTIGATION OF SOME PROPERTIES OF PHENYLHYDRAZINE AND FACTORS AFFECTING HYDRAZONE FORMATION

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This work was undertaken as a necessary preliminary to the evolution of a general iodimetric method for the estimation of carbonyl group content in organic compounds.

Iodine reacts with phenylhydrazine giving iodobenzene and hydriodic acid.[1] $C_6H_5NH.NH_2 + 2I_2 = C_6H_5I + 3HI + N_2$.

Consistent iodine values can readily be obtained for aqueous phenylhydrazine solutions, but only under certain conditions. The iodobenzene produced dissolves some iodine. The simplest method of titration is to add an excess of iodine, allow sufficient time for complete reaction, add an excess of thiosulfate, shake with a few cubic centimeters of ether, and finally titrate with iodine once more, using freshly prepared starch solution. Shaking with ether hastens the extraction of the iodine from the iodobenzene and hence expedites the determination. The ether does not affect the titration.

The presence of the sodium acetate[2] or other "buffer" salts usually recommended such as sodium bicarbonate, borate or phosphate, slows down the reaction and gives low results. Addition of hydrochloric or

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[1] von Meyer, *J. prakt. Chem.*, [2] **36,** 115 (1887).

[2] Fischer, *Ber.*, **17,** 572 (1884); **41,** 74 (1908).