LXV.—*The Inhibitory Effect of Substituents in Chemical Reactions. Part I. The Reactivity of the Amino-group in Substituted Arylamines.*

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IN a study of the effect of substituents of different polar and steric character in certain organic chemical reactions, the first problem which it appeared desirable to investigate was the effect on the reactivity of the amino-group in substituted anilines; for this purpose, the reaction by which we have synthesised numerous thiocarbimides and thiocarbamides (J., 1924, **125**, 1702; *J. Soc. Chem. Ind.*, 1926, **45**, 83T; *Rec. trav. chim.*, 1926, **45**, 421) appeared well suited.

A primary amine can react with thiocarbonyl chloride to give two substances. The primary product is a thiocarbamyl chloride (equation A). This, in the presence of water, normally loses hydrogen chloride, yielding the corresponding thiocarbimide (equation B). When, however, inhibitory groups are present, the thiocarbamyl chloride loses hydrogen chloride with considerable reluctance and reacts with a second molecule of the amine to give the *s*-diarylthiocarbamide (equation C).

$$NH_2R + CSCl_2 = NHR{\cdot}CSCl + HCl \quad . \quad . \quad (A)$$

$$NHR{\cdot}CSCl \xrightarrow{H_2O} RNCS + HCl \quad . \quad . \quad . \quad (B)$$

$$NHR{\cdot}CSCl + NH_2R = CS(NHR)_2 + HCl \quad . \quad . \quad . \quad (C)$$

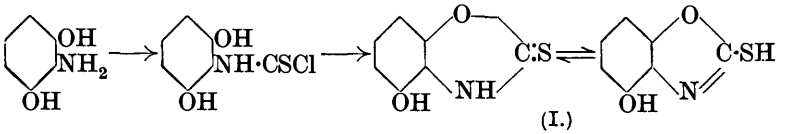
The ability of the thiocarbamyl chloride to eliminate hydrogen chloride is therefore a measure of the influence of the substituent on the reactivity of the original amine. When several inhibitory groups are present, as, for instance, in *s*-tribromoaniline and 2 : 4 : 6-trinitroaniline, inhibition of the reaction (A) may take place.

The various arylamines were treated with excess of thiocarbonyl chloride in the presence of water under standard conditions. When the amine was reactive, as in the nuclear methyl-substitution derivatives of aniline, the reaction was usually complete in 10 minutes and the thiocarbimide was isolated in 80—90% yield. When slight inhibition was present, as in the monochloroanilines (Dyson, George, and Hunter, J., 1926, 3041), thiocarbimide formation took place to the extent of about 60—70%, but the reaction was much slower, requiring about 30 minutes. When the reactivity of the amino-group was considerably depressed, as in anthranilic acid, the reaction with thiocarbonyl chloride was exceedingly slow and the only isolable product was the *s*-diarylthiocarbamide. With substances such as 2 : 6-dichloroaniline, no reaction whatever took place under these conditions; such amines were also recovered unchanged after being heated at 180° with thiocarbonyl chloride under pressure.

The experiments described in this paper are not a crucial test of the reactivity of arylamines, but are merely preliminary experiments carried out in connexion with a comprehensive study of the inhibition of organic reactions; the quantitative results will be published later.

The experiments of Dyson and Hunter (*J. Soc. Chem. Ind.*, 1926, **45**, 83T) have shown that no possible combination of nuclear methyl groups appreciably affects the reactivity of the amino-group towards thiocarbonyl chloride, the three toluidines, *o*-4-, *m*-4-, and *p*-xylidines, ψ-cumidine, mesidine, and aminopentamethylbenzene all giving nearly quantitative yields of the corresponding thiocarbimides. We have since found that *o*-3- and *m*-2-xylidines also behave normally in this respect.

The effect of a hydroxyl group in the ortho-position to the amino-group cannot be directly determined, since it reacts with the chlorine atom of the intermediate thiocarbamyl chloride with the formation of a 1-thiobenzoxazole. Its effect on the amino-group appears, however, to be slight, since 2 : 6-dihydroxyaniline reacts readily with thiocarbonyl chloride, giving 3-hydroxy-1-thiobenzoxazole (I).



(I.)

The methoxy- and the ethoxy-group also have only a slight inhibitory effect on the amino-group, since the three anisidines, 3 : 4-, 2 : 5-, and 2 : 6-dimethoxyanilines, and the three phenetidines

all react normally with thiocarbonyl chloride, giving the corresponding thiocarbimides.

The effect of the cyano-group appears to lie between those of the alkyloxy-groups and the halogens, since *m*- and *p*-cyanoanilines and 2 : 5-dicyanoaniline react fairly readily, giving the corresponding cyano-substitution derivatives of phenylthiocarbimide.

Chlorine atoms considerably depress the reactivity of the amino-group in the chloroanilines; two *o*-chlorine atoms are necessary, however, for complete inhibition (Dyson, George, and Hunter, *loc. cit.*). Since the reaction becomes progressively easier with *o*-chloroaniline, *o*-bromoaniline, and *o*-iodoaniline, the effect of a halogen substituent is clearly due to a combination of both steric and polar effects. Indeed, the reaction between thiocarbonyl chloride and *o*-iodoaniline is very vigorous and is accompanied by a considerable evolution of heat (almost sufficient in our experiments to cause the supernatant water to boil). The hindering effect of an *o*-halogen atom does not appear to be affected by replacement of the second *o*-hydrogen atom by a methyl group, since 3 : 5-dibromo-*o*-toluidine reacted normally with thiocarbonyl chloride, giving 3 : 5-*dibromo*-o-*tolylthiocarbimide*, under conditions in which the isomeric 2 : 4 : 6-tribromo-*m*- and 3 : 5-dibromo-*p*-toluidines were recovered unchanged.

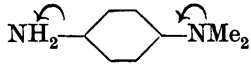
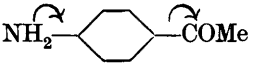
The effect of the nitro-group is very similar to that of the chlorine atom : *o*-, *m*-, and *p*-nitrophenylthiocarbimides were obtained from the corresponding nitroanilines with some difficulty, and complete inhibition was observed in the cases of 2 : 4- and 2 : 6-dinitroanilines and 2 : 4 : 6-trinitroaniline. On the other hand, 3 : 5-dinitroaniline reacted with thiocarbonyl chloride with difficulty, giving s-*bis*-3 : 5-*dinitrophenylthiocarbamide*. So far as we are aware, this is the first recorded instance of a 2 : 4-disubstituted benzene derivative being less reactive than the 3 : 5-isomeride. Further confirmation of the marked inhibitory effect of *o*-halogeno- and of nitro-substituents was obtained by an examination of 3-nitro-*o*-toluidine and 2-nitro-*p*-phenetidine, which reacted sluggishly with thiocarbonyl chloride, giving the corresponding thiocarbimides, and of 2 : 6-dichloro-, 2 : 6-dibromo-, and 2 : 6-di-iodo-*p*-nitroanilines, 4 : 6-dibromo-*o*-nitroaniline, and 2 : 4 : 6-tribromo-*m*-nitroaniline, with all of which complete inhibition was observed.

These results throw grave doubt on the theory of steric hindrance which attributes inhibition to the decrease of free space caused by the substituent (Henry, *Ber.*, 1877, **10**, 2041; Wegscheider, *Monatsh.*, 1895, **16**, 137; Angeli, *Atti R. Accad. Lincei*, 1896, **1**, 84), particularly since the molecular volumes of the methoxy- (37·1) and the methyl (25·5) group (Le Bas, " The Molecular Volumes of

Liquid Chemical Compounds ") are considerably greater than the atomic volume (22·1) of chlorine.

Finally the effects of acidic and basic groups were studied. The sulpho- and the carboxyl group both exert strong inhibitory actions, the former being the more powerful, since sulphanilic acid could not be induced to react with thiocarbonyl chloride, whereas anthranilic acid was very slowly converted into s-*di*-o-*carboxyphenylthiocarbamide*.

The experiments of Billeter and Steiner (*Ber.*, 1887, **20**, 228) indicate that there is no appreciable steric hindrance due to the amino-groups in the phenylenediamines. Acylation of one amino-group, however, depresses the reactivity of the other, since s-*di*-p-*acetamidophenylthiocarbamide* is the only product isolable from *p*-aminoacetanilide and thiocarbonyl chloride and is only formed very slowly in the presence of water at 100°. Alkylation has little effect on the amino-group, since *as*-dimethyl-*p*-phenylenediamine readily passes into p-*dimethylaminophenylthiocarbimide* under the usual conditions. This would appear to be explicable on the " electron sink " properties of the carbonyl group (Allan, Oxford, Robinson, and Smith, J., 1926, 401), in which case the effect would be expected to be still more strikingly manifested in *p*-aminoacetophenone as shown in the formulæ (II) and (III).

(II.)   (III.)

p-Aminoacetophenone, however, reacts with thiocarbonyl chloride under the usual conditions with the greatest ease, giving a 70% yield of the corresponding thiocarbimide.

A point of interest in connexion with the organoleptic properties of thiocarbimides is that the *o*-substituted derivatives usually have an unpleasant pungent odour, whereas the *p*-substituted derivatives are invariably associated with the pleasant odour of aniseed.

Experimental.

Rapid Thiocarbimide Formation.

The thiocarbimides described below were usually obtained as follows : Thiocarbonyl chloride (1·3 mols.) was completely suspended in water (10 vols.) at 15° by vigorous stirring during the addition of a solution of the arylamine (1 mol.) in chloroform (5 vols.). After 15 minutes' stirring, the chloroform layer was removed and dried with calcium chloride, and the solvent and the excess of thiocarbonyl chloride were distilled off on a steam-bath. The thiocarbimide was obtained either by fractionating (under reduced or atmospheric

pressure according to the nature of the compound) or by steam-distilling the residue.

The arylthiocarbamides, $NHAr{\cdot}CS{\cdot}NH_2$, were prepared from the respective thiocarbimides and warm alcoholic ammonia, and the *s*-diarylthiocarbamides, $CS(NHAr)_2$, by condensing the thiocarbimides (1 mol.) with the corresponding arylamines (1 mol.) in alcohol.

m-*Xylyl-2-thiocarbimide* was obtained from *m*-2-xylidine by fractionation of the residue after removal of the solvent and the excess of thiocarbonyl chloride, and distilled as a colourless oil, b. p. 247°/760 mm. (Found: S, 19·8. C_9H_9NS requires S, 19·6%). m-*Xylyl-2-thiocarbamide* crystallised from alcohol in minute, square prisms, m. p. 190° (Found: S, 19·0. $C_9H_{12}N_2S$ requires S, 18·8%). s-*Di*-m-*xylyl-2-thiocarbamide* crystallised in glistening, flat plates, m. p. 208° (Found: S, 11·4. $C_{17}H_{20}N_2S$ requires S, 11·3%).

o-*Xylyl-3-thiocarbimide* was obtained from *o*-3-xylidine (0·75 g.) and isolated by microdistillation as a colourless oil of pungent odour, b. p. 262—263°/760 mm. (yield, 0·8 g.). o-*Xylyl-3-thiocarbamide* crystallised from alcohol in brilliant, white needles, m. p. 182° (Found: S, 18·5%).

o-*Anisylthiocarbimide* was obtained from *o*-anisidine, and distilled as a pale yellow oil of unpleasant odour, b. p. 266—267°/760 mm. (Found: S, 19·2. C_8H_7ONS requires S, 19·4%). o-*Anisylthiocarbamide* crystallised in white needles, m. p. 148—149° (Found: S, 17·2. $C_8H_{10}ON_2S$ requires S, 17·6%). s-*Di*-o-*anisylthiocarbamide* formed glistening prisms, m. p. 134° (Found: S, 11·0. $C_{15}H_{16}O_2N_2S$ requires S, 11·1%).

m-*Anisylthiocarbimide* was prepared from *m*-anisidine and distilled as a colourless oil of pungent odour, b. p. 267°/760 mm. (Found: S, 19·3%). m-*Anisylthiocarbamide* crystallised in glistening prisms, m. p. 160° (Found: S, 17·0%). s-*Di*-m-*anisylthiocarbamide* separated from alcohol in clear, crystalline plates, m. p. 126° (Found: S, 13·2%).

p-Anisylthiocarbimide is a pale yellow oil having a pleasant odour of aniseed, b. p. 280—281°/760 mm. *p*-Anisylthiocarbamide forms small prisms, m. p. 211°, and *s*-di-*p*-anisylthiocarbamide, small, glistening plates, m. p. 187°.

2 : 5-Dimethoxyaniline was most conveniently prepared as follows: A solution of quinol (20 g.) in 35% potassium hydroxide was treated with 50 c.c. of methyl sulphate, giving 24 g. of *p*-dimethoxybenzene, m. p. 56°; this was converted into 2 : 5-dimethoxynitrobenzene by nitration with nitric acid (*d* 1·2) in glacial acetic acid, and the nitro-derivative reduced with tin and hydrochloric acid. The dimethoxyaniline, isolated by means of ether, separated from dilute alcohol in small crystals, m. p. 84° (Magatti, *Ber.*, 1881,

14, 71; Baessler, *Ber.*, 1884, **17**, 2119). The compound rapidly turned red on exposure to the atmosphere.

2 : 5-*Dimethoxyphenylthiocarbimide.*—The dark-coloured mixture obtained on addition of the dimethoxyaniline (8 g.) to thiocarbonyl chloride in water was steam-distilled, and the distillate extracted with chloroform, yielding the thiocarbimide in large crystals, m. p. 32° (to an oil of pungent odour). 2 : 5-*Dimethoxyphenylthiocarbamide* forms small crystals, m. p. 161°, from alcohol (Found : S, 15·3. $C_9H_{12}O_2N_2S$ requires S, 15·1%). s-*Bis*-2 : 5-*dimethoxyphenylthiocarbamide* forms small crystals, m. p. 127° (Found : S, 9·3. $C_{17}H_{20}O_4N_2S$ requires S, 9·2%).

3 : 4-*Dimethoxyphenylthiocarbimide* was obtained from 3 : 4-dimethoxyaniline (prepared from 4-nitroveratrole) as an oil of pungent odour similar to that of phenylthiocarbimide; it could not be crystallised (Found : S, 17·0. $C_9H_9O_2NS$ requires S, 16·4%). 3 : 4-*Dimethoxyphenylthiocarbamide* separated from alcohol as a microcrystalline powder, m. p. 234° (Found : S, 15·0%). s-*Bis*-3 : 4-*dimethoxyphenylthiocarbamide* formed white prisms, m. p. 140°.

o-*Ethoxyphenylthiocarbimide* was obtained from *o*-phenetidine, as a pale yellow oil, b. p. 273—275°/760 mm. (Found : S, 18·0. C_9H_9ONS requires S, 17·9%). o-*Ethoxyphenylthiocarbamide* crystallised from dilute alcohol in small crystals, m. p. 126° (Found : S, 16·5. $C_9H_{12}ON_2S$ requires S, 16·3%). s-*Di*-o-*ethoxyphenylthiocarbamide*, after three recrystallisations from dilute alcohol, formed large prisms, m. p. 125° (Found : S, 10·0. $C_{17}H_{20}O_2N_2S$ requires S, 10·2%).

m-*Ethoxyphenylthiocarbimide* was obtained from *m*-phenetidine as a clear, colourless oil of pungent odour, b. p. 278°/758 mm. (Found : S, 17·8%). m-*Ethoxyphenylthiocarbamide* formed short, white prisms, m. p. 167° (Found : S, 16·6%). s-*Di*-m-*ethoxyphenylthiocarbamide* separated from alcohol in aggregates of coarse needles, m. p. 115° (Found : S, 10·0%).

p-Ethoxyphenylthiocarbimide forms large, glistening plates having the odour of aniseed, m. p. 76°. *p*-Ethoxyphenylthiocarbamide forms small crystals, m. p. 176°, and *s*-di-*p*-ethoxyphenylthiocarbamide, plates, m. p. 171°.

o-*Carbethoxyphenylthiocarbimide.*—The rate of addition of ethyl anthranilate solution in chloroform to the thiocarbonyl chloride suspension was adjusted so that the temperature did not rise above 30°. The thiocarbimide distilled under reduced pressure as a pale, thick oil of nauseating odour, b. p. 150—151°/1 mm. (Found : S, 15·0. Calc. for $C_{10}H_9O_2NS$: S, 15·4%). *o*-Carbethoxyphenylthiocarbamide separated from 50% alcohol in needles, m. p. 300—305° (Found : S, 14·2. Calc. for $C_{10}H_{12}O_2N_2S$: S, 14·3%).

s-Di-*o*-carbethoxyphenylthiocarbamide crystallised slowly from

its solutions in colourless prisms which decomposed without melting (Found: S, 8·0. Calc. for $C_{19}H_{20}O_4N_2S$: S, 8·6%).

m-*Carbethoxyphenylthiocarbimide* distilled as a pale yellow oil, b. p. 152°/10 mm. (Found: S, 15·2%). m-*Carbethoxyphenylthiocarbamide* formed long, glistening prisms, m. p. 294—295° (Found: S, 14·2%). s-*Di*-m-*carbethoxyphenylthiocarbamide* separated from alcohol in white prisms which decomposed without melting (Found: S, 8·0%). This compound was sometimes difficult to crystallise.

p-*Carbethoxyphenylthiocarbimide* crystallised from dilute alcohol in glistening plates having an odour of aniseed, m. p. 58° (Found: S, 15·3%). p-*Carbethoxyphenylthiocarbamide* formed glistening needles, m. p. 159° (Found: S, 14·0%). s-*Di*-p-*carbethoxyphenylthiocarbamide* crystallised in small prisms, m. p. 165° (Found: S, 9·0%).

p-*Dimethylaminophenylthiocarbimide* was prepared from *as*-dimethyl-*p*-phenylenediamine and thiocarbonyl chloride in the usual way; after removal of the chloroform on a steam-bath, the residue was steam-distilled for 8—10 hours, the thiocarbimide slowly passing over as an oil which solidified in pale yellow prisms, m. p. 67° (Found: S, 18·2. $C_9H_{10}N_2S$ requires S, 17·9%). p-*Dimethylaminophenylthiocarbamide* formed pale yellow prisms, m. p. 190° (Found: S, 16·0. $C_9H_{13}N_3S$ requires S, 16·4%).

p-*Acetylphenylthiocarbimide* was prepared from *p*-aminoacetophenone in the same way as the dimethylaminophenyl compound, and distilled slowly in steam as a solid of pronounced aniseed odour. It crystallised in broad plates (yield, 70%), m. p. 76° (Found: S, 18·0. C_9H_7ONS requires S, 18·1%). p-*Acetylphenylthiocarbamide* formed small, yellow prisms, m. p. 215° (decomp.) (Found: S, 16·8. $C_9H_{10}ON_2S$ requires S, 16·5%). s-*Di*-p-*acetylphenylthiocarbamide* crystallised in sparingly soluble, microscopic crystals, m. p. 198° (Found: S, 10·0. $C_{17}H_{16}O_2N_2S$ requires S, 10·8%).

Retarded Thiocarbimide Formation.

In the preparation of the thiocarbimides described below, the mixture was stirred for 30 minutes after the addition of the solution of the amine.

m-Nitrobenzonitrile (m. p. 116°; prepared by the nitration of benzonitrile) (14 g.) was warmed with tin (40 g.) and concentrated hydrochloric acid (100 c.c.), the reaction mixture treated with excess of 20% sodium hydroxide, and *m*-cyanoaniline extracted with ether; after recrystallisation from alcohol, this had m. p. 52°.

m-*Cyanophenylthiocarbimide* was obtained as an oil of pungent odour which decomposed on heating to 250°. m-*Cyanophenylthiocarbamide* crystallised in long needles, m. p. 137° (Found: S, 18·0. $C_8H_7N_3S$ requires S, 18·0%). s-*Di*-m-*cyanophenylthiocarbamide*

separated from alcohol in small, cream-coloured crystals, m. p. 144° (Found : S, 11·0. $C_{15}H_{10}N_4S$ requires S, 11·5%).

p-*Cyanophenylthiocarbimide* was obtained by steam-distilling the residue obtained after removal of the chloroform and the excess of thiocarbonyl chloride; on recrystallisation from dilute alcohol it formed glistening, fibrous needles having a strong odour of aniseed, m. p. 45° (Found : S, 19·6. $C_8H_4N_2S$ requires S, 20·0%).

p-*Cyanophenylthiocarbamide* separated from dilute alcohol in prisms, m. p. 169° (Found : S, 18·2%). s-*Di*-p-*cyanophenylthiocarbamide* formed white crystals, m. p. 171° (Found : S, 11·6%).

2 : 5-Dicyanoaniline was prepared as follows : *p*-Dicyanobenzene (prepared from *p*-cyanoaniline by the Sandmeyer reaction) (25 g.) was nitrated with nitric acid (*d* 1·5) at 80° for 20 minutes; a considerable portion of the material was oxidised to benzoquinone. On pouring the nitration product into cold water and extracting the product with ligroin (in which benzoquinone is almost insoluble), 5 g. of the required 2 : 5-dicyanonitrobenzene were obtained, which, on reduction with tin and hydrochloric acid, yielded the dicyanoaniline. On recrystallisation, the amine formed small, brown crystals, m. p. 62°. The yield was 1·5 g.

2 : 5-*Dicyanophenylthiocarbimide*, after recrystallisation from alcohol, retained a strong almond-like odour; it decomposed without melting (Found : S, 17·4. $C_9H_3N_3S$ requires S, 17·3%). 2 : 5-*Dicyanophenylthiocarbamide* separated from alcohol in needles, m. p. 228°.

o-*Bromophenylthiocarbimide* distilled as a colourless oil of pungent odour, b. p. 257°/770 mm. o-*Bromophenylthiocarbamide* separated from alcohol in rosettes of glistening, rhombic prisms, m. p. 125° (Found : S, 14·0. $C_7H_7N_2BrS$ requires S, 13·9%). s-*Di*-o-*bromophenylthiocarbamide* formed long needles, m. p. 157° (Found : S, 9·0. $C_{13}H_{10}N_2Br_2S$ requires S, 8·3%).

2 : 5-*Dibromophenylthiocarbimide* was obtained from 2 : 5-dibromoaniline as a clear oil, b. p. 240°, which formed a glacial mass of needles on cooling; m. p. 17—18° (Found : S, 11·2. $C_7H_3NBr_2S$ requires S, 10·9%). 2 : 5-*Dibromophenylthiocarbamide* formed long needles, m. p. 130° (Found : S, 10·5. $C_7H_6N_2Br_2S$ requires S, 10·3%). s-*Di*-2 : 5-*dibromophenylthiocarbamide*, after two recrystallisations from dilute alcohol, had m. p. 154° (Found : S, 6·0. $C_{13}H_8N_2Br_4S$ requires S, 5·9%).

o-*Iodophenylthiocarbimide* formed long, slender needles having a pungent odour, m. p. 39°. o-*Iodophenylthiocarbamide* separated from alcohol in broad plates, m. p. 157° (Found : S, 11·0. $C_7H_7N_2IS$ requires S, 11·5%). s-*Di*-o-*iodophenylthiocarbamide* separated from dilute alcohol in small, ill-defined crystals, m. p. 164° (decomp.).

m-*Iodophenylthiocarbimide* formed glistening needles, m. p. 46° (Found : S, 12·4. C_7H_4NIS requires S, 12·2%). m-*Iodophenylthiocarbamide* crystallised in white needles, m. p. 160° (decomp.) (Found : S, 11·8%).

3 : 5-*Dibromo*-o-*tolylthiocarbimide.*—The dibromotoluidine (10 g.) was shaken with water and thiocarbonyl chloride, and the mixture steam-distilled; the thiocarbimide was then obtained as a white solid of pungent odour. On recrystallisation from dilute alcohol, it formed a pasty mass of crystals, m. p. about 25°, b. p. 280° (Found : S, 10·0. $C_8H_5NBr_2S$ requires S, 10·5%).

3-*Nitro*-o-*tolylthiocarbimide.*—3-Nitro-*o*-toluidine (10 g.) was refluxed with thiocarbonyl chloride (10 g.) for 10 minutes, and the excess of thiocarbonyl chloride removed in steam. The residue, on recrystallisation from glacial acetic acid, yielded the thiocarbimide in lemon-yellow plates, m. p. 69° (Found : S, 16·1. $C_8H_6O_2N_2S$ requires S, 16·5%).

2-*Nitro*-4-*ethoxyphenylthiocarbimide.*—Ten g. of 2-nitro-*p*-phenetidine were gradually added to a suspension of thiocarbonyl chloride (10 g.) in water (300 c.c.). The thiocarbimide, isolated in the same way as the nitrotolyl compound, crystallised from glacial acetic acid in flat, orange plates, m. p. 78° (Found : S, 14·4. $C_9H_8O_3N_2S$ requires S, 14·3%). 2-*Nitro*-4-*ethoxyphenylthiocarbamide* separated from alcohol in glistening, orange-brown crystals, m. p. 177° (Found : S, 13·0. $C_9H_{11}O_3N_3S$ requires S, 13·3%).

Thiocarbamide Formation.

s-*Bis*-3 : 5-*dinitrophenylthiocarbamide.*—3 : 5-Dinitroaniline (10 g.) was shaken with thiocarbonyl chloride (11 g.) in water (150 c.c.) for ½ hour and the excess of thiocarbonyl chloride was then removed in steam. The residue, after several recrystallisations from light petroleum–acetic acid, gave the thiocarbamide in minute, yellow prisms, m. p. 160° (Found : S, 7·5. $C_{13}H_8O_8N_6S$ requires S, 7·8%).

s-*Di*-o-*carboxyphenylthiocarbamide.*—Anthranilic acid (50 g.) was refluxed with thiocarbonyl chloride (50 g.) and water (300 c.c.) for 42 hours, and the excess of chloride removed by steam distillation. The residue was extracted with a large volume of alcohol; the thiocarbamide was then obtained as a granular powder. After several recrystallisations from alcohol (animal charcoal) it was obtained in small crystals, m. p. 300° (decomp.) (Found : S, 10·0. $C_{15}H_{12}O_4N_2S$ requires S, 10·1%).

s-*Di*-p-*acetamidophenylthiocarbamide* was obtained from *p*-aminoacetanilide (20 g.) in the same way as the dicarboxyphenylthiocarbamide, and crystallised in small prisms, m. p. 220° (decomp.) (Found : S, 8·8. $C_{17}H_{18}O_2N_4S$ requires S, 9·3%).

Inhibition.

2 : 6-Dichloro-, -dibromo-, -di-iodo-*p*-nitroanilines, 4 : 6-dibromo-*o*-nitroaniline, and 2 : 4 : 6-tribromo-*m*-nitroaniline were all prepared by the methods given in the literature; they were recovered unchanged after treatment with thiocarbonyl chloride and water and identified by m. p. and mixed m. p. determinations. Sulphanilic acid was recovered unchanged after being refluxed with excess of thiocarbonyl chloride and water for 3 hours and identified by its properties, analysis (Found : S, 18·6%), and by the formation of Orange II on diazotisation and coupling with β-naphthol.

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