[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

# Thiocarbanilide Formation under Different Conditions

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One object of this work was to obtain material with which to test further the observations of Raiford and Daddow,[1] who found that *sym*-diphenylurea and thiocarbanilide, respectively, react with phenylhydrazine to give the corresponding 1,4-diphenylsemicarbazide, as indicated.[2]

$$(C_6H_5NH)_2CS + H_2NNHC_6H_5 \longrightarrow C_6H_5NHCSNHNHC_6H_5 + C_6H_5NH_2$$

It was soon found that anilines with substituents in other than ortho positions[3] gave little or no thiocarbanilide by the method usually described in books of preparation.[4] Thus, 3-nitro-, 3,5-dichloro-, 3,4- and 3,5-dibromoanilines gave no product when treated for several hours according to method 1 (see below), while with method 3 the yields were 87, 71, 47 and 85%, respectively. On the other hand, with method 1, the yields of thiocarbanilide from *m*-xylidine (1,2,4:NH$_2$ = 1), 2-methoxy-5-methylaniline, 2-aminodiphenyl and 2-amino-4′-chlorodiphenyl were 84, 10, 84 and 63%. Since steric hindrance could not account for these differences, a comparative study of four methods of preparation was made, in which aniline and twenty-nine of its substitution products were used.

## Experimental Part

### Starting Materials

**2-Methoxy-4-bromo-5-methylphenylamine.**—To a solution of 15 g. of 2-acetylamino-*p*-cresyl methyl ether, m. p. 111°,[5] dissolved in 50 cc. of acetic acid, one molecular proportion of bromine in acetic acid was slowly added with stirring, and after thirty minutes the mixture was poured into water; yield, 88%. Crystallization from ligroin gave colorless needles of m. p. 122–123°.

*Anal.* Calcd. for $C_{10}H_{12}O_2NBr$: Br, 30.97. Found: Br, 31.00.

To obtain the free amine the acetyl derivative was boiled under reflux for an hour with concentrated hydrochloric acid, the mixture made alkaline with sodium hydroxide and distilled with steam; yield, 98%. Crystallization from ligroin gave long, nearly colorless needles of m. p. 96°.

*Anal.* Calcd. for $C_8H_{10}ONBr$: Br, 37.00. Found: Br, 36.97.

TABLE I

SUBSTITUTED ANILINES

| Substituents | Yield, % | Solvent | Crystal form | M. p., °C. | Formula | N Analyses, % Calcd. | N Analyses, % Found |
|---|---|---|---|---|---|---|---|
| 3-Methyl-4-acetylamino- | 74 | Water | Nearly colorless needles | 129[a]–130 | $C_9H_{12}ON_2$ | 17.07 | 17.17 |
| 2-Bromo-4-acetylamino- | 71 | Alcohol | Colorless needles | 129–130 | $C_8H_9ON_2Br$ | 12.22 | 12.10 |
| 3-Bromo-4-acetylamino- | 41[b] | Alcohol | Fine needles | 210–211 | $C_8H_9ON_2Br$ | 12.22 | 12.17 |
| 3,5-Dibromo-4-acetylamino-[c] | 78 | Alcohol | Nearly colorless prisms | 244–245 | $C_8H_8ON_2Br_2$ | 9.09 | 9.11 |
| 2-(4-Chlorophenyl)-[d] | 61 | Ligroin | Irregular crystalline masses | 52 | $C_{12}H_{10}NCl$ | 6.88 | 6.54[e] |

[a] While this work was in progress, Elson, Gibson and Johnson [*J. Chem. Soc.*, 2739 (1929)] recorded 143° for a product that was reported to have the structure of this one.

[b] This refers to purified material.

[c] Obtained by reduction of 2,6-dibromo-4-nitroacetanilide which, in turn, was prepared by a modification of Körner and Contardi's method [*Chem. Zentr.*, **84**, Pt. 3, 1039 (1913)] to the extent that acetylation was accomplished by treatment of a hot acetic acid suspension of the nitroaniline with acetyl chloride.

[d] Obtained in 61% yield by reduction of 2-nitro-4′-chlorodiphenyl, donated by the Federal Phosphorus Company, to whom we here express our thanks.

[e] Checked by analysis for chlorine. Calcd. for $C_{12}H_{10}NCl$: Cl, 17.44. Found: Cl, 16.95.

**Preparation of other Amines.**—With the exceptions indicated below the amines used in this work are on record. The new ones were prepared as follows. In the cases of the monophenyl derivatives an intimate mixture of about three parts of the nitro compound and two parts of powdered iron was added slowly to about twenty parts of boiling 50% alcohol containing 1% of acetic acid, the mixture heated under reflux and stirred for one to two hours longer, then made alkaline with ammonia water, boiled for a few minutes and filtered at once. Concentration of the filtrate gave the desired product, which was crystallized from a suitable solvent. When diphenyl

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(1) Raiford and Daddow, THIS JOURNAL, **53**, 1553 (1931).

(2) Walther [*J. prakt. Chem.*, [2] **53**, 468 (1896); **74**, 228 (1906)] previously heated thiocarbanilide with an excess of phenylhydrazine and noted the formation of diphenylthiosemicarbazide along with nitrogen, ammonia and hydrogen sulfide. No substituted thiocarbanilides were tested, and aniline was not noted as a product except at 165–170° in sealed tubes where it was probably formed by decomposition of the excess of phenylhydrazine.

(3) Kauffmann and Franck [*Ber.*, **40**, 4007 (1907)] found that anilines with substituents in the 2,6-positions gave very small yields of thiocarbanilide by the usual method, while Dyson, George and Hunter [*J. Chem. Soc.*, 437 (1927)] and Naunton [*J. Soc. Chem. Ind.*, **45**, 376T (1926)] obtained the lowest yields with similarly substituted amines when thiocarbonyl chloride was the reagent.

(4) Hoffman, *Ann.*, **70**, 144 (1849); Dennstedt, *Ber.*, **13**, 230 (1880); Hugershoff, *ibid.*, **32**, 2246 (1899).

(5) Limpach [*Ber.*, **22**, 349 (1889)] recorded 110°.

TABLE II

COMPOSITION AND PROPERTIES OF *sym*-DIARYLTHIOUREAS

| Substituents, phenyl | Yield,[a] % | Solvent | Crystal form | M. p., °C. | Formula | Analyses Halogen Calcd. | Analyses Halogen Found | Analyses Nitrogen, % Calcd. | Analyses Nitrogen, % Found |
|---|---|---|---|---|---|---|---|---|---|
| 3,5-Dibromo- | 85 | Dil. alc. | Colorless needles | 134–135 | $C_{13}H_8N_2Br_4S$ | 58.82 | 58.26 | 5.14 | 5.07 |
| 3,4-Dibromo- | 47 | Alcohol | Cream plates[b] | 100–103 | $C_{13}H_8N_2Br_4S$ | 58.82 | 60.97 | .. | .. |
| 2,5-Dichloro- | 68[c] | Benzene | Colorless fibrous masses | 175–176 | $C_{13}H_8N_2Cl_4S$ | ... | ... | .. | .. |
| 2,4-Dichloro- | 79 | Benzene | Brown plates | 184–185 | $C_{13}H_8N_2Cl_4S$ | 38.79 | 38.70 | .. | .. |
| 3,5-Dichloro- | 71 | Dil. alc. | Colorless powder | 156–157 | $C_{18}H_8N_2Cl_4S$ | 38.79 | 38.66 | 7.65 | 7.30 |
| 2-Bromo-4-chloro- | 64 | Alcohol | Colorless fluffy masses | 206–207 | $C_{18}H_8N_2Cl_2Br_2S$ | 50.76 | 50.78 | 6.15 | 6.24 |
| 2-Chloro-4-bromo- | 65 | Benzene | Pale brown plates | 159–160 | $C_{13}H_8N_2Cl_2Br_2S$ | 50.76 | 50.58 | .. | .. |
| 2-Methoxy-5-methyl- | 72 | Alcohol | Stout needles | 143–144 | $C_{17}H_{20}O_2N_2S$ | ... | ... | 8.86 | 8.83 |
| 2-Methoxy-4-bromo-5-methyl- | 62 | Alcohol[d] | Colorless powder | 175–176 | $C_{17}H_{18}O_2N_2Br_2S$ | 33.75 | 33.70 | 5.90 | 5.91 |
| Diphenyl | | | | | | | | | |
| 4-Amino- | 90 | Alcohol[d] | Colorless plates | 230 | $C_{25}H_{20}N_2S$ | ... | ... | 7.36 | 7.23 |
| 4′-Chloro-4-amino- | 88 | Alcohol[d] | Colorless irregular masses | 219–220 | $C_{25}H_{18}N_2Cl_2S$ | 15.81 | 15.48 | 6.23 | 6.13 |
| 2-Amino- | 90 | Dil. alc. | Colorless irregular masses | 154–155 | $C_{25}H_{20}N_2S$ | ... | ... | 7.36 | 7.05 |
| 4′-Chloro-2-amino- | 70 | Alcohol | Colorless needles | 193–194 | $C_{25}H_{18}N_2Cl_2S$ | ... | ... | 6.23 | 6.11 |

[a] With one exception Fry's method gave the highest yields, and those were recorded.

[b] Obtained by spontaneous evaporation of solvent at room temperature. Repeated attempts to crystallize from various solvents failed to give a pure product.

[c] Previously prepared by Noelting and Kopp [*Ber.*, **38**, 3507 (1905)] who recorded no yield, but analyzed the product.

[d] Purified by extraction of foreign matter with alcohol.

derivatives were prepared, the method was modified as suggested by Jenkins, McCullough and Booth.[6] Analytical data and properties are given in Table I.

**Methods Tested.**—1. A mixture of 10 g. of the amine, 2 molecular proportions of carbon disulfide, 25 cc. of alcohol and 0.5 g. of sulfur was placed in a round-bottomed flask connected by a ground-glass joint to a reflux condenser and heated to gentle boiling as long as hydrogen sulfide was evolved. The volatile material was then distilled off, the residue freed from starting material and crystallized from a suitable solvent.

2. To 10 g. of the amine in 30 cc. of alcohol and 1.5 molecular proportions of carbon disulfide, 0.2 g. of powdered sodium hydroxide was added and the mixture heated for four hours. Volatile material was removed by steam distillation, and the residue purified as indicated.

3. The method developed by Fry[7] was modified to the extent that the mixture was stirred mechanically until the reaction was completed, in order to prevent the carrying down of iodine as the pyridinium iodide precipitated.

4. The method described by Snedker[8] was followed here with the exception that the mixture was shaken[9] instead of stirred, as suggested by the author. Even then, in some instances, especially with solid amines, unsatisfactory results were obtained, probably due to the difficulty in mixing the components.

Table II gives the properties and analytical data for the new thioureas obtained.

## Summary

1. Several methods for the preparation of thiocarbanilide have been studied.

2. Many anilines that contain no ortho substituent failed to give thiocarbanilide with the method commonly described in books of preparation, while others with one ortho substituent did react. With methods 2 and 3 the greater number of these gave satisfactory yields of product. When the nitro group was present in position 2 or 4 no thiocarbanilide was obtained by any method tried. Steric hindrance does not account for these differences.

3. In Fry's method the precipitation of pyridinium iodide tended to carry down unchanged iodine, and thus prolong the experiment. Stirring the mixture hastened the reaction.

4. Snedker's method was not generally satisfactory with solid amines due, possibly, to the difficulty in maintaining intimate contact between reactants.

5. Further work is in progress.

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(6) Jenkins, McCullough and Booth, *Ind. Eng. Chem.*, **22**, 33 (1930).

(7) Fry, THIS JOURNAL, **35**, 1544 (1913).

(8) Snedker, *J. Soc. Chem. Ind.*, **44**, 486T (1925).

(9) Voorhees with Adams, THIS JOURNAL, **44**, 1403 (1922).