3-(2-Bromo-4-chloroanilino)-4-bromo-5-phenylpyrazole.—An insoluble salt separated from a chloroform solution of III on the addition of an excess of bromine dissolved in chloroform. It was decomposed by hot alcohol, from which the new substance separated as needles, m. p. 198–199°.

Anal. Calcd. for $C_{15}H_{10}Br_2ClN_3$: Br, 37.4. Found: Br, 37.1.

Phenylpropiol-3-chlorothioanilide.—Prepared from *m*-chlorophenyl isothiocyanate, it was purified in small lots by crystallization from chloroform–petroleum ether mixtures. Tiny yellow needles were obtained which melted with decomposition at 115–116°.

Anal. Calcd. for $C_{15}H_{10}ClNS$: C, 66.3; H, 3.7. Found: C, 66.8; H, 3.7.

It was readily polymerized by heating an ether solution with a few drops of sodium hydroxide solution. The new substance separated in the form of brown crystals, melting with decomposition at 227–228°.

Anal. Calcd. for $(C_{15}H_{10}ClNS)x$: C, 66.3; H, 3.7. Found: C, 66.3; H, 3.7.

Summary

Phenyl propiol-chlorothioanilide, prepared by the interaction of sodium phenylacetylene and *p*-chlorophenyl isothiocyanate, reacts with hydroxylamine and hydrazine. The resulting isoxazole and pyrazole form substitution products with bromine, chlorine and nitric acid.

MEDFORD, MASS. RECEIVED OCTOBER 24, 1938

[A CONTRIBUTION FROM PEARSON MEMORIAL LABORATORY, TUFTS COLLEGE]

Reactions of Phenylpropiol-4-iodoanilide and Similar Thioamides

BY DAVID E. WORRALL, MORRIS LERNER AND JOHN WASHNOCK, JR.

In a previous investigation[1] it was shown that the isoxazole and pyrazole obtained from the condensation of phenylacetylene with phenyl isothiocyanate form substitution products with chlorine, bromine and nitric acid. The reaction has been investigated further in order to find the scope, for it not only offers a new approach to the isoxazole or pyrazole series but also furnishes a new series of derivatives.

Theoretically, substitution in these compounds may occur in the phenyl, anilino and pyrazole or isoxazole rings. Actually, as the presence of benzoic acid[1] among the oxidation products of a halogenated isoxazole indicated, reactivity is confined to the anilino or heterocyclic ring or both. That the latter group is involved follows from the fact that the thioamide obtained from *p*-bromoisothiocyanate formed an isoxazole isomeric with that resulting from the bromination of anilinophenylisoxazole.[1] It also follows that substitution starts with the isoxazole ring and at position 4. The oxidation of the tribromo derivative of the corresponding pyrazole[1] produced 2,4-dibromoaniline which fits in with this picture and which also indicates that the anilino group reacts in the orthodox manner with bromine. It has been assumed that similar relations exist with the substances investigated in the present communication.

(1) THIS JOURNAL, 60, 1198 (1938).

Experimental

The thioamides were prepared through the interaction of sodium phenylacetylene suspended in ether with the appropriate isothiocyanate. The product after standing for several hours was filtered and cautiously decomposed with ice water and dilute acid. Since these amides are easily destroyed even by moderate heating, the crude product after thorough washing with cold alcohol was used for the experimental work. Small portions were purified for analysis by the use of chloroform–petroleum ether mixtures. Save for the 4-phenyl derivative which formed bright yellow plates, pale yellow needles were obtained. All melted with decomposition. Yields (60–80%) were satisfactory except for the phenethyl derivative. The substances were polymerized by heating ether solutions in the presence of a few drops of concd. sodium hydroxide solution. Brown or greenish-brown irregular platelets formed which melted with decomposition.

TABLE I

ANILINE SUBSTITUTED PHENYLPROPIOL THIOANILIDES

Subs.	M. p., °C.	Formula	Analyses, % Calcd.	Found
4-Iodo	140–141	$C_{15}H_{10}INS$	8.8	8.8
Dimer	Indefinitely above 173	$(C_{15}H_{10}INS)x$	8.8	8.8
4-Ethoxy	111–112	$C_{17}H_{15}NOS$	11.4	11.4
Dimer	199–200	$(C_{17}H_{15}NOS)x$	11.4	11.4
3-Bromo	120–121	$C_{15}H_{10}BrNS$	10.1	10.4
Dimer	Indefinite	$(C_{15}H_{10}BrNS)x$	10.1	10.1
4-Phenyl	128–129	$C_{21}H_{15}NS$	10.2	10.4
Dimer	230–232	$(C_{21}H_{15}NS)x$	10.2	9.7
α-Naphthylamide	184–185	$C_{19}H_{13}NS$	11.2	10.9

The isoxazoles were obtained by gradually adding the thioamide to an excess of hydroxylamine in hot alcohol until evolution of hydrogen sulfide stopped. The dark colored solution was then concentrated to a small volume.

TABLE II

-5-PHENYLISOXAZOLE

Subs.	M. p., °C.	Formula	Analyses, % Calcd.	Found
3-(4-Iodoanilino)-	148–149	$C_{15}H_{11}IN_2O$	I, 35.5	I, 35.4
3-(4-Iodoanilino)-4-bromo-[2]	172–173	$C_{15}H_{10}BrIN_2O$	Br, 18.1	Br, 18.5
3-(4-Iodoanilino)-4-chloro-	151–152	$C_{15}H_{10}ClIN_2O$	Cl, 8.9	Cl, 8.6
3-(4-Iodoanilino)-4-nitro-	243–244	$C_{15}H_{10}IN_3O_3$	I, 31.2	I, 31.6
3-(2-Bromo-*p*-toluidino)-4-bromo-	130–131	$C_{16}H_{12}Br_2N_2O$	Br, 39.2	Br, 38.8
3-(2,6-Dichloro-*p*-toluidino)-4-chloro-	229–230	$C_{16}H_{11}Cl_3N_2O$	Cl, 30.1	Cl, 29.7
3-(4-Phenylanilino)-	176–177	$C_{21}H_{16}N_2O$	C, 80.5	C, 80.1
			H, 4.8	H, 4.5

TABLE III

-5-PHENYLPYRAZOLE

Subs.	M. p., °C.	Formula	Analyses, % Calcd.	Found	Calcd.	Found
3-(4-Iodoanilino)-	175–176	$C_{15}H_{12}IN_3$	I, 35.1	I, 35.3		
3-(2-Bromo-4-iodoanilino)-4-bromo-	201–202	$C_{15}H_{10}Br_2IN_3$	Br, 30.8	Br, 30.8		
3-(4-Iodoanilino)-4-chloro-	206–207	$C_{15}H_{11}IN_3Cl$	Cl, 8.9	Cl, 8.5		
3-(3-Bromoanilino)	205–206	$C_{15}H_{12}BrN_3$	Br, 25.5	Br, 25.4		
3-(3-Bromoanilino)-4-bromo-	178–179	$C_{15}H_{11}Br_2N_3$	Br, 40.7	Br, 40.5		
3-(*p*-Toluidino)-	157–158	$C_{16}H_{15}N_3$	C, 77.1	C, 76.8	H, 6.1	H, 5.9
3-(2-Bromo-*p*-toluidino)-4-bromo-	181–182	$C_{16}H_{13}Br_2N_3$	Br, 39.4	Br, 39.5		
3-(2,6-Dinitro-*p*-toluidino)-4-nitro-	245–247	$C_{16}H_{12}N_6O_6$	C, 50.0	C, 49.9	H, 3.1	H, 3.0
3-(4-Phenylanilino)	219–220	$C_{21}H_{17}N_3$	C, 81.1	C, 80.9	H, 5.5	H, 5.3

The product contained tarry material best removed by ethylene chlorohydrin after which it was crystallized from alcohol several times, eventually separating as nearly colorless needles; yield 20–30%. Bromine and chlorine reacted smoothly in chloroform solution, producing after crystallization from alcohol colorless hair-like crystals. The toluidino derivative separated as plates. The nitration went less smoothly, while the products separated from glacial acetic acid as yellow crystals. Only slight evidence of isoxazole formation was found with the naphthyl or the phenetidine derivatives.

Pyrazole formation was also accompanied by considerable tar formation, best purified in the manner indicated for the isoxazoles and forming eventually colorless needles or plates. The chlorine and bromine derivatives were obtained in good yield as colorless needle-like crystals. Nitration did not go so smoothly, the products apparently consisting of mixtures not easily separated.

(2) The value for bromine was reached by first subtracting from the weight of the mixed silver halides the theoretical value for silver iodide.

Summary

Certain derivatives of 3-anilino-5-phenylisoxazole and -pyrazole have been prepared and their reactions with chlorine, bromine and nitric acid studied.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

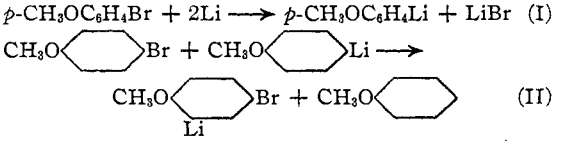
Metalation as a Side Reaction in the Preparation of Organolithium Compounds

BY HENRY GILMAN, WRIGHT LANGHAM AND ARTHUR L. JACOBY

Introduction

It was reported recently that the extent of metalation of dibenzothiophene by a series of organolithium compounds varied quite regularly with the rates of cleavage of organometallic compounds by hydrogen chloride. In that study, *p*-methoxyphenyllithium behaved anomalously, for the acid obtained subsequent to carbonation was 5-bromo-2-methoxybenzoic acid. This acid undoubtedly was formed from 5-bromo-2-methoxyphenyllithium, which in turn was formed, in all probability, by auto-metalation in accordance with the following sequence of reactions[1]

$$p\text{-}CH_3OC_6H_4Br + 2Li \longrightarrow p\text{-}CH_3OC_6H_4Li + LiBr \quad (I)$$



(II)

That is, part of the original *p*-bromoanisole was metalated as a side reaction in the preparation of

(1) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938). See p. 109 of that article for the identification of 2-methoxy-5-bromobenzoic acid and for the mechanism of its formation.