[CONTRIBUTION FROM THE PRIVATE LABORATORY OF J. P. WETHERILL]

2-Methyl- and 2-Ethyl-4-(*p*-halogenphenyl)-thiazoles and some of their Derivatives

BY J. P. WETHERILL AND RAYMOND M. HANN

The relatively high toxicity of certain sulfur compounds for mosquito larvae of the culicine group has been indicated by Campbell, Sullivan, Smith and Haller.[1]

In this connection certain derivatives of benzothiazole exhibited considerable larvicidal action and it seems possible that compounds of the simpler thiazole skeleton would yield interesting results. We have therefore prepared a series of 2-methyl- and 2-ethylthiazoles containing also various *p*-halogenated phenyl groups in the 4 position. The later changes in structure would seem desirable in view of the increased toxicity of chlorinated benzothiazoles in comparison with the unsubstituted benzothiazole.

For the synthesis of the thiazoles the classic method of Hantzsch of interaction of halogenated ketones with thioamides in their tautomeric form has been employed. The 2-methyl-4-phenylthiazole has been prepared by Hantzsch[2] and the 2-ethyl-4-phenyl homolog by Hubacher[3] from ω-bromoacetophenone, thioacetamide and thiopropionamide. By employing the *p*-halogen phenacyl chlorides we have extended the series of known derivatives and obtained the synthetic products desired for tests as larvicides. The reaction is:

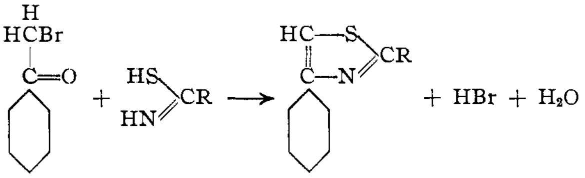

TABLE I

2-METHYL AND 2-ETHYL-4-*p*-HALOGEN-PHENYLTHIAZOLES

Thiazole	Formula	Appearance	M. p., °C. (corr.)	Analyses, % Kjeldahl-Gunning-Arnold method Calcd.	Found
2-Methyl-4-*p*-chlorophenyl[a]	$C_{10}H_8NSCl$	Colorless, brilliant, shimmering plates	122–123	6.68	6.71
2-Methyl-4-*p*-bromophenyl	$C_{10}H_8NSBr$	Colorless, soft micaceous scales	134	5.51	5.57
2-Methyl-4-*p*-iodophenyl	$C_{10}H_8NSI$	Slight yellow brilliant elongated thin plates	138	4.65	4.60
2-Ethyl-4-*p*-chlorophenyl	$C_{11}H_{10}NSCl$	Colorless elongated plates	72	6.26	6.31
2-Ethyl-4-*p*-bromophenyl	$C_{11}H_{10}NSBr$	Colorless, flat terminated plates	86	5.22	5.26
2-Ethyl-4-*p*-iodophenyl	$C_{11}H_{10}NSI$	Colorless glistening needles	99	4.45	4.42

[a] The hydrobromide of this base crystallizes in colorless glistening platelets melting at 186–187° (corr.).

Experimental

The thioamides were obtained from the Eastman Kodak Company; ω-bromo-*p*-chloroacetophenone was prepared as directed by Hann, Reid and Jamieson,[4] and the other halogenated phenacyl chlorides were prepared in yields of over 90% from halogen benzenes and chloroacetyl chloride by the Friedel-Crafts synthesis with the technical assistance of H. P. Newton.

The thiazoles were obtained by refluxing twentieth molar quantities of the thioamides with the appropriately substituted ω-halogen-*p*-halogen phenyl ketone in sufficient 95% alcohol to maintain solution (usually 150 cc.) for fifteen minutes, filtering the hot solution through norite and allowing to crystallize. A second crop was obtained by adding water to the warm filtrate just to turbidity and allowing to cool slowly. In the case of 2-methyl-4-*p*-chlorophenylthiazole the base hydrobromide crystallized, but in all other experiments the free base was obtained under these conditions. The thiazoles were recrystallized from alcohol to constant melting point and analyzed. The yields were 85 to 95%. The properties of the compounds are listed in Table I.

The picrates were prepared by dissolving 1 g. of free base and 1.5 g. of picric acid in 40 cc. of 95% alcohol. The picrate which separated on cooling was recrystallized from 95% alcohol to constant melting point.

The mercuri-chlorides were obtained by dissolving 1 g. of the base in 10 cc. of 1:1 hydrochloric acid and adding 2 g. of solid mercuric chloride to the solution. They were recrystallized from a solution containing 5 g. of mercuric chloride, 5

---

[1] Campbell, Sullivan, Smith and Haller, unpublished results, to appear in *J. Ec. Entomology*.

[2] Hantzsch, *Ann.*, **250**, 269 (1889).

[3] Hubacher, *ibid.*, **259**, 231 (1890).

[4] Hann, Reid and Jamieson, THIS JOURNAL, **52**, 819 (1930).

TABLE II

PICRATES OF 2-METHYL AND 2-ETHYL-4-*p*-HALOGEN-PHENYLTHIAZOLES

Thiazole picrate	Formula	Appearance	M. p., °C. (corr.)	Analyses Kjeldahl–Gunning–Arnold method Calcd.	Found
2-Methyl-4-*p*-chlorophenyl	$C_{16}H_{11}O_7N_4SCl$	Yellow microcrystalline powder	163	12.77	12.80
2-Methyl-4-*p*-bromophenyl	$C_{16}H_{11}O_7N_4SBr$	Yellow glistening triclinic plates	160	11.60	11.70
2-Methyl-4-*p*-iodophenyl	$C_{16}H_{11}O_7N_4SI$	Yellow flat platelets	152	10.57	10.60
2-Ethyl-4-*p*-chlorophenyl	$C_{17}H_{13}O_7N_4SCl$	Yellow very fine acicular needles	143–144	12.38	12.21
2-Ethyl-4-*p*-bromophenyl	$C_{17}H_{13}O_7N_4SBr$	Yellow brilliant slender needles	143	11.27	11.25
2-Ethyl-4-*p*-iodophenyl	$C_{17}H_{13}O_7N_4SI$	Yellow shining microcrystalline plates	148	10.30	10.62

TABLE III

2-METHYL AND 2-ETHYL 4-*p*-HALOGEN-PHENYL THIAZOLE MERCURI-CHLORIDES

Thiazole mercuri-chloride	Formula	Appearance	M. p., °C. (corr.)	Analyses, % Kjeldahl–Gunning–Arnold method Calcd.	Found
2-Methyl-4-*p*-chlorophenyl	$C_{10}H_8NSCl\cdot HgCl_2$	Colorless brilliant microcrystalline prisms	202–203	2.91	2.85
2-Methyl-4-*p*-bromophenyl	$C_{10}H_8NSBr\cdot HgCl_2$	Colorless somewhat opaque needles	221	2.66	2.79
2-Methyl-4-*p*-iodophenyl	$C_{10}H_8NSI\cdot HgCl_2$	Colorless shining needles	235	2.45	2.57
2-Ethyl-4-*p*-chlorophenyl	$C_{11}H_{10}NSCl\cdot HgCl_2$	Colorless somewhat opaque long needles	164	2.83	3.12
2-Ethyl-4-*p*-bromophenyl	$C_{11}H_{10}NSBr\cdot HgCl_2$	Colorless chalky microcrystalline powder	177	2.60	2.57
2-Ethyl-4-*p*-iodophenyl	$C_{11}H_{10}NSI\cdot HgCl_2$	Colorless glistening needles	188	2.34	2.27

cc. of concd. hydrochloric acid, 100 cc. of water and 100 cc. of 95% alcohol. The crystals were washed with this solution, as water tended to precipitate salt from the mother liquor and rendered the crystals opaque. The physical properties are summarized in Table III.

Summary

Thioacetamide and thiopropioamide have been condensed with a series of *p*-halogen phenacyl chlorides to yield the corresponding 2-methyl and 2-ethyl-4-*p*-halogen-phenylthiazoles.

The thiazoles have been characterized by preparation of their picrates and mercuri-chlorides.

2819 McGILL TERRACE
WASHINGTON, D. C.

RECEIVED JANUARY 8, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ARKANSAS]

Preparation of N-Benzoyl-*o*-aminobenzenesulfonamide. Condensation to Heterocyclic Compounds[1]

BY E. WERTHEIM

Previous work in this Laboratory has shown that diphenic sulfinide (diphensaccharin) (I) cannot be formed by the internal condensation of N-*o*-chlorobenzoyl-*o*-chlorobenzenesulfonamide.[2] In the present work the synthesis was attempted by the diazotization of N-benzoyl-*o*-aminobenzenesulfonamide (II), followed by various procedures to obtain the loss of nitrogen and ring closure. Difficulties were experienced in diazotizing due to the great tendency of (II) to lose water to form 3-phenyl-1,2,4-isobenzothiodiazine-1-dioxide (III). This occurred, for instance, when an alcoholic solution of (II) was saturated with hydrogen chloride.

With diazotization methods which avoided this difficulty ring closure produced not a seven- but a six-atom ring. The compound secured was an isomer of diphensaccharin, 3-phenyl-1,4,2-benzothioxazine-1-dioxide (IV). Analyses and molecular weight determinations confirm the proposed structure of (IV) as well as the following facts: the compound is insoluble in alkali and does not acetylate; mild hydrolysis yields a compound whose analysis agrees with that of the predicted

---

[1] Paper No. 340, Journal Series, University of Arkansas.

[2] Wertheim, THIS JOURNAL, **53**, 1172 (1931).