TABLE III[a]

PHENOLBETAINES OBTAINED BY TREATING *cis*- AND *trans*-STYRYL-TYPE DYES WITH SODIUM OR AMMONIUM HYDROXIDE

Phenol-betaine	Yield, %	M.P., °C.	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	λ mμ	ε
From IA	95	240–275 (dec.)	$C_{22}H_{18}N_2O$	80.98	81.19	5.52	5.54	8.59	8.27	245 462 560	28,620 18,940 26,480
Dihydrochloride		262 (dec.)	$C_{22}H_{18}N_2O \cdot 2HCl$					7.02	6.61		
From IB[b]	80	189–190	$C_{22}H_{18}N_2O$	80.98	80.70	5.52	4.42	8.59	9.09	250 372	33,760 27,680
Dihydrochloride		299 (dec.)	$C_{22}H_{18}N_2O \cdot 2HCl$					7.02	6.98		
From IIIB[c]	70	182–183	$C_{20}H_{19}NO_2$	78.69	78.91	6.22	5.36	4.59	4.82	362	24,900
Dihydrochloride		259 (dec.)	$C_{20}H_{19}NO_2 \cdot HCl$					3.98	4.21		

[a] All hydrochlorides crystallized from dilute hydrochloric acid as orange yellow needles. [b] Made by subjecting IB (0.2 g.) to Method A except that methanol (10 ml.) was used instead of water. It crystallized from ethanol as light yellow prisms. [c] Made by similar treatment of IIIB (0.2 g.) as that used for IB or subjecting it to Method B except that methanol was used instead of water.

Treatment of styryl-type dyes with sodium or ammonium hydroxide. Phenolbetaine from IA (Method A). To a mixture of IA (0.2 g.) and water (4 ml.) 5% sodium hydroxide (4 ml.) was added dropwise with stirring, the resulting solution heated at around 80° for 20 min. until a thick paste of fine blue crystals formed, water added, carbon dioxide introduced until a color reaction to phenolphthalein disappeared, the separated crystals filtered, washed with water, and crystallized from ethanol to yield fine violet blue needles. It showed an ill-defined melting point, softened or foamed at about 140°, melted at 240–270° (dec.). After drying at room temperature over potassium hydroxide it retained 3 moles of water of crystallization.

Anal. Calcd. for $C_{22}H_{18}N_2O \cdot 3H_2O$: C, 69.47; H, 6.32; N, 7.37. Found: C, 68.89; H, 7.04; N, 7.53.

(Method B.) To a mixture of IA (0.2 g.) and water (10 ml.), 14% ammonium hydroxide (2 g.) was added dropwise with stirring. The resulting deep blue violet solution separated blue crystals on standing. After standing overnight, the excess ammonia was removed on a water bath, the crystals filtered, washed with water, and recrystallized from ethanol.

On treating IIIA with methanolic ammonium hydroxide, the initial material was recovered, melting point and mixed melting point with a sample of IIIA 258° (dec.). Treatment with sodium hydroxide or silver oxide in methanol also failed to produce the desired phenolbetaine.

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N-Aroxyacetyl-*N*-arylglycines

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Since the discovery of the usefulness of some aroxyacetic acids as plant growth substances, a large number of their amides have been synthesized[1] and tested for such activity. As the appropriate *N*-arylglycines themselves exhibit the activity,[2] it also seems of significance to test *N*-aroxyacetyl-*N*-arylglycine, an *N*-aryl substituted aroxyacetamide, for the study of structure-activity relationship of plant growth substances. The present report describes the preparations of eighteen new compounds with the above-mentioned structure by Schotten-Baumann reaction.

In Table I, the melting points and the analyses of these compounds are summarized. Wood and Fontaine[3] have used this method successfully in the synthesis of halogenated phenoxyacetyl derivatives of several amino acids. We also obtained the aroxyacetyl derivatives of *N*-(*p*-tolyl)glycine as well as those of *N*-(3-chloro-*p*-tolyl)glycine in good yields; however, the aroxyacetylations of other glycines gave lower ones.

None of these compounds had auxin properties in the Went pea test or in the Aduki test,[4] while in the *Avena* cylinder test, as shown in Table I, the 2,4-dichloro and 4-chlorophenoxyacetyl derivatives of six *N*-arylglycines exhibited the activity which seemed to be related both to the activity of the parent aroxyacetic acid and to that of the corresponding glycine although they were less active. The details of the biological test will be reported elsewhere.

EXPERIMENTAL

Six *N*-arylglycines used in this work were prepared in our laboratory by saponifying the corresponding nitriles with a 5% aqueous sodium hydroxide solution. Three acid chlorides were prepared by treating one mole of each acid with three moles of thionyl chloride according to the

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(1) (a) M. S. Newman, W. Fones, and M. Renoll, *J. Am. Chem. Soc.*, **69**, 718 (1947); (b) A. G. Norman, *Botan. Gaz.*, **107**, 476 (1946).

(2) A. Takeda and J. Senda, *Ber. Ohara Inst. landw. Biol.*, **11**, 1 (1957).

(3) J. W. Wood and T. D. Fontaine, *J. Org. Chem.*, **17**, 891 (1952).

(4) The test using a large bean variety of *Phaseolus angularis* W. F. Wight (Aduki beans) called "Dainagon" as test materials, A. Takeda and J. Senda, *loc. cit.* These results have been rather unexpected ones, because it is well-known that the amides whose parent acids possess the activity are active likewise.

TABLE I

$R_1OCH_2CO\overset{R_2}{\overset{|}{N}}CH_2COOH$ N-AROXYACETYL-N-ARYLGLYCINES[a]

R_1	R_2	Yield, %	M.p.,[b] (dec.) °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found[c]	Activity[d]
2,4-$Cl_2C_6H_3$	3,4-$Cl_2C_6H_3$	18	183–183.5	$C_{16}H_{11}Cl_4NO_4$	3.31	3.2	10^{-7}–10^{-6}
	4-ClC_6H_4	28	156–158	$C_{16}H_{12}Cl_3NO_4$	3.60	3.5	10^{-6}
	3-ClC_6H_4	19	140–141	$C_{16}H_{12}Cl_3NO_4$	3.60	3.5	10^{-6}
	3-Cl-4-$CH_3C_6H_3$	50	163–164	$C_{17}H_{14}Cl_3NO_4$	3.48	3.4	10^{-6}
	4-$CH_3C_6H_4$	64	171–172	$C_{17}H_{15}Cl_2NO_4$	3.80	3.8	10^{-6}
	C_6H_5	38	164–165	$C_{16}H_{13}Cl_2NO_4$	3.95	3.9	10^{-6}
4-ClC_6H_4	3,4-$Cl_2C_6H_3$	19	103–104	$C_{16}H_{12}Cl_3NO_4$	3.60	3.5	10^{-6}
	4-ClC_6H_4	20	162–163	$C_{16}H_{13}Cl_2NO_4$	3.95	3.9	10^{-6}–10^{-5}
	3-ClC_6H_4	7	118–119	$C_{16}H_{13}Cl_2NO_4$	3.95	3.9	10^{-6}
	3-Cl-4-$CH_3C_6H_3$	61	128–129	$C_{17}H_{15}Cl_2NO_4$	3.80	3.7	10^{-5}
	4-$CH_3C_6H_4$	86	166–167	$C_{17}H_{16}ClNO_4$	4.19	4.1	10^{-5}
	C_6H_5	36	114–115	$C_{16}H_{14}ClNO_4$	4.38	4.2	10^{-6}–10^{-5}
2-Cl-4-$CH_3C_6H_3$	3,4-$Cl_2C_6H_3$	48	162–164	$C_{17}H_{14}Cl_3NO_4$	3.48	3.5	10^{-5}
	4-ClC_6H_4	65	164–165	$C_{17}H_{15}Cl_2NO_4$	3.80	3.9	Inactive
	3-ClC_6H_4	27	176–177	$C_{17}H_{15}Cl_2NO_4$	3.80	3.8	Inactive
	3-Cl-4-$CH_3C_6H_3$	86	178–179	$C_{18}H_{17}Cl_2NO_4$	3.66	3.6	Inactive
	4-$CH_3C_6H_4$	79	170–171	$C_{18}H_{18}ClNO_4$	4.03	4.0	Inactive
	C_6H_5	25	130–133	$C_{17}H_{16}ClNO_4$	4.19	4.1	Inactive

[a] All the compounds listed here are new. [b] Melting points are uncorrected. [c] Analyzed by modified semimicro Kjeldahl, A. Takeda and J. Senda, *Ber. Ohara Inst. landw. Biol.*, *10*, 241 (1956). [d] Activity in the *Avena* cylinder test. These figures mean the approximate values of the minimum threshold concentrations (mole/liter) to induce the lengthwise elongation of *Avena* (oats var. Victory) coleoptile cylinders 10 mm. long. They have been estimated graphically through the concentration-elongation curves in each testings. The acids being difficultly soluble in water, the diethylamine salts of these compounds have been prepared and used for the biological experiments. The preparations will be published elsewhere. Activities in the same test for the parent acids are as follows: 10^{-7} for 2,4-dichlorophenoxyacetic acid; 10^{-6} for 4-chlorophenoxyacetic acid and *N*-(3,4-dichlorophenyl)glycine; 10^{-6}–10^{-5} for *N*-(4-chlorophenyl)glycine; 10^{-5}–10^{-4} for *N*-(3-chloro-4-methylphenyl)glycine and *N*-(3-chlorophenyl)glycine; 10^{-4} for *N*-(*p*-tolyl)glycine and *N*-phenylglycine.

statement of the literature.[5] Unreported before is 2-chloro-4-methylphenoxyacetyl chloride. This new compound was obtained as a colorless liquid distilling at 155–157°/24 mm. in a yield of 94% on the basis of 0.25 mole of the acid. It occasionally crystallized at room temperature. The melting point of the crude product was 31–34°.

Anal. Calcd. for $C_9H_8Cl_2O_2$: Ionizable Cl, 16.20. Found: Cl, 15.86.

The aroxyacetylation was carried out in the same manner as described by Wood and Fontaine using 0.02 mole of *N*-arylglycine in general. The following experiments illustrate the procedures used.

N-(2-Chloro-4-methylphenoxyacetyl)-N-(p-tolyl)glycine. Into a solution of 3.3 g. of *N*-(*p*-tolyl)glycine (0.02 mole) in 120 ml. of 0.5*N* aqueous sodium hydroxide a solution of 4.4 g. or 0.02 mole of 2-chloro-4-methylphenoxyacetyl chloride in 20 ml. of benzene was added with rapid stirring at about 10° and the stirring was continued for an additional hour. The benzene layer was extracted once with 50 ml. of water. The extract and the aqueous layer were combined. The combined solution was then acidified with a diluted hydrochloric acid (1:1) until blue to Congo Red. The 2-chloro-4-methylphenoxyacetyl derivative, which soon separated as white fine needles, was filtered with suction, washed several times with water, and dried at 60–70° for 24 hr. The yield of the crude product was 6.5 g. (94%), m.p. 158–162°; one recrystallization from dilute alcohol (1:1) gave 5.5 g. (79%) of a pure product, m.p. 169–171°, which was further recrystallized for analysis and showed the m.p. of 170–171° with slight decomposition.

N-(2,4-Dichlorophenoxyacetyl)-N-(3,4-dichlorophenyl)glycine. The reaction was carried out as usual except that it was continued for 2 hr. by using 0.04 mole of the glycine and twofold of other reactants. The oily material, which first precipitated on acidifying the aqueous layer, solidified after being allowed to stand overnight. This crude product was treated as follows, since it hardly gave a definite melting point even after several recrystallizations from various solvents (dilute alcohol, benzene, ligroin, and acetic acid). To the clear solution of the crude product in 40 ml. of a 1*N* aqueous sodium hydroxide a 20% aqueous sodium hydroxide was added until a slight turbidity occurred. Chilling the resulted solution to about 5° in an ice bath, the sodium salt of *N*-(2,4-dichlorophenoxyacetyl)-*N*-(3,4-dichlorophenyl)glycine was separated on the bottom as a sirupy precipitate. It was collected by decantation and redissolved in a small amount of water. On acidifying the latter solution, a gummy material, which soon solidified, was obtained. One recrystallization of this product from dilute alcohol (1:1) afforded 3.0 g. (18%) of crystals melting at 182–184° with slight decomposition, m.p. 182–183.5° after two further recrystallizations from dilute alcohol. From the supernatant fluid 5.2 g. (59% of the used amount) of 2,4-dichlorophenoxyacetic acid was recovered.

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[5] H. Freed, *J. Am. Chem. Soc.*, 68, 2112 (1946).