acetone. It was recrystallized from methanol–ether and appeared as colorless needles, m. p. 188–190° (dec.).

*Anal.* Calcd. for $C_{15}H_{23}ClI_3NO$: C, 27.73; H, 3.57. Found: C, 27.63; H, 3.85.

The acetone mother liquors of the hydrochloride deposited colorless crystals of another hydrochloride on standing, which melted at 160–170° (dec.). This compound could not be purified further.

**2,4,6-Triiodophenyl Chloroacetate.**—A solution of 2.9 g. of 2,4,6-triiodophenol and 3 g. of chloroacetic anhydride in 10 cc. of pyridine was allowed to stand overnight and then poured into 100 cc. of water. A crystalline precipitate and a brown tar were formed; the latter went slowly into solution. The crystals were filtered, washed, and recrystallized from boiling ethanol. The product crystallized as shining blades, m. p. 141–142°.

*Anal.* Calcd. for $C_8H_4ClI_3O_2$: C, 17.52; H, 0.74. Found: C, 17.76; H, 1.19.

## Summary

2,4-Diiodophenylsulfanilamide, 2,4-diiodophenylglycine and 2,4-diiodophenylurea have been prepared from 2,4-diiodoaniline. A series of 2,4,6-triiodophenyl dialkylaminoalkyl ethers has also been synthesized. The failure of 2,4,6-triiodoaniline to take part in certain reactions has been discussed.

A study of the application of several of these compounds to X-ray visualization and chemotherapy is in progress.

UNIVERSITY, VIRGINIA RECEIVED JANUARY 29, 1941

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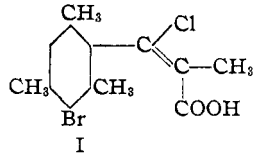
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

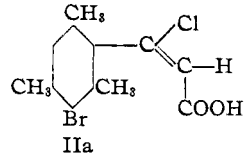
# Restricted Rotation in Aryl Olefins. II. Preparation and Resolution of Certain β-Chloro-β-(2,4,6-trimethyl- and 2,4,6-triethyl-3-bromophenyl)-acrylic Acids

BY ROGER ADAMS, A. W. ANDERSON[1] AND M. W. MILLER[1]

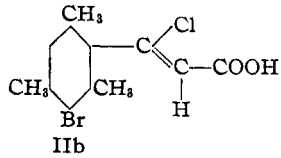
The observation that β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid (I) could be resolved and that the optically active forms were very stable to racemization was reported in a previous paper.[2] The study of several analogous compounds now has been completed; they are shown by formulas II–VII.



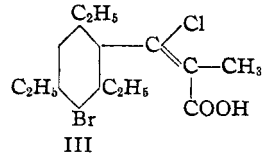
I



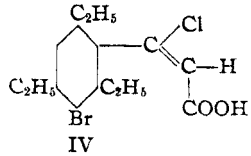
IIa



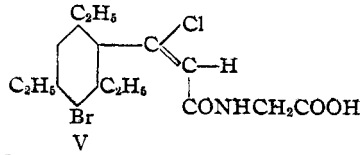
IIb



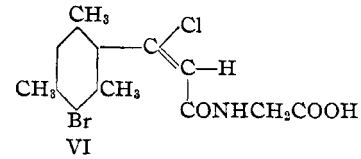
III



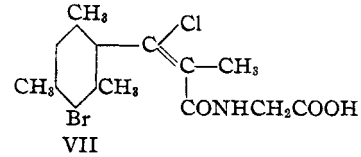
IV



V



VI



VII

Compounds I and II differ merely by a methyl and hydrogen in the α-position to the carboxyl group. Compound I showed no signs of racemization after boiling for fifteen hours in ethanol or *n*-butanol. Compound II, on the other hand, though stable in boiling ethanol, slowly racemized in boiling *n*-butanol with a half-life of approximately two hundred minutes. Geometric forms of compound I and compound II theoretically are capable of existence but only a single form was isolated in either case and all attempts to prepare the isomers failed. It is reasonable to assume that molecules I and II have the same configuration.

The active isomers of the *cis*- and *trans*-forms (IIa and IIb) should have a marked difference in optical stability, for molecule IIa resembles more closely a 2,2′,6,6′-tetrasubstituted biphenyl and IIb a trisubstituted biphenyl. The latter are decidedly more labile than the former and in aryl

(1) An abstract of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry. Eastman Kodak Fellows, 1939–1940, 1940–1941.

(2) Adams and Miller, THIS JOURNAL, **62**, 53 (1940).

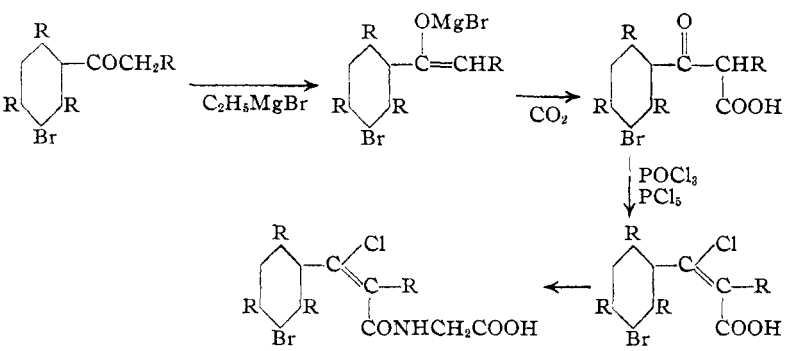
olefins, where mobility is surely greater than in biphenyls, it would appear doubtful whether a molecule of structure IIb could have the stability observed in the compound obtained in the laboratory. A study of Stuart models of these molecules confirms this postulation. On the basis of this reasoning, β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic acid was assumed to have structure IIa and β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid, because it was prepared in a similar manner, structure I.

The study of the triethylbenzene derivatives was undertaken in order to compare the stability of analogous molecules in which the larger ethyl groups replace the methyls in the benzene ring. As was anticipated, the active forms of compound III could not be racemized. The acid (IV) homologous with compound III in that the α-methyl group to the carboxyl is replaced by a hydrogen atom was readily prepared but all attempts to obtain a satisfactory salt for resolution failed. As a consequence, the acid (IV) was converted to the acid chloride and condensed with glycine to yield compound V which offered no difficulties in resolution. Its optically active forms were perfectly stable under conditions which resulted in the racemization of compound IIa. It is impossible to say whether the ethyl groups or the glycine residue was the chief contributing factor to the greater stability of V over IIa.

The study of the glycine (VI) of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic acid (IIa) leads to surprising results. The compound (VI) was resolved and the rate of racemization of the active form was greater (one hundred and thirty-three minutes in boiling butanol) than that of the active form of the substance (IIa) from which it was derived (two hundred minutes in boiling butanol). Although the determination of the half-life periods in boiling butanol involves a large experimental error so that these figures are somewhat in error quantitatively, the relative stabilities are certainly correct qualitatively. That no rearrangement had taken place about the double bond during the formation of the glycine (VI) from the acid (IIa) was demonstrated by hydrolysis of the glycine to the original acid IIa.

In substituted biphenyls, the increase of the size of the 2-substituted group, for example from methoxyl to propoxyl, causes an increase in the stability of the molecule. From the experiments just cited in these particular aryl olefins, the opposite effect obtains. Here, the larger group may be reducing the symmetry of the molecule and thereby increasing mobility which allows more ready slippage of the interfering groups by each other. The glycine (VII) derived from the acid (I) was resolved and the active form did not racemize in boiling butanol.

The compounds described in this communication were made by the general procedure shown below.[2]




## Experimental

Bromomesitylene was prepared according to directions given in Organic Syntheses[3] and bromo-2,4,6-triethylbenzene according to the procedure of Fuson and Corse.[4]

The preparation of the acyl derivatives of these compounds, from them the keto acids and finally the chloro acids was carried out in exactly the same way as previously described for conversion of bromopropiomesitylene to β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid.[2]

**Bromoacetomesitylene.**—From 100 g. of bromomesitylene, 300 g. of carbon disulfide, 140 g. of anhydrous aluminum chloride and 53 g. of acetic anhydride was obtained 83 g. (68%) of bromoacetomesitylene; colorless liquid, b. p. 114–115° (3 mm.); $n^{20}D$ 1.5550; $d^{20}_{20}$ 1.2774.

*Anal.* Calcd. for $C_{11}H_{13}OBr$: C, 54.77; H, 5.49. Found: C, 54.64; H, 5.58.

**2,4,6-Trimethyl-3-bromobenzoylacetic Acid.**—From 23 g. of bromoacetomesitylene was obtained 12 g. (44%) of 2,4,6-trimethyl-3-bromobenzoylacetic acid; white crystals from benzene, m. p. 98–99° (cor.) with decomposition.

*Anal.* Calcd. for $C_{12}H_{13}O_3Br$: C, 50.52; H, 4.56. Found: C, 51.01; H, 4.72.

**β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl-acrylic Acid (IIa).**—From 10 g. of the crude benzoylacetic acid was obtained 4.5 g. (41%) of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic acid; white needles from

(3) "Organic Syntheses," Vol. XI, 1931, p. 24.
(4) Fuson and Corse, THIS JOURNAL, **60**, 2063 (1938).

petroleum ether (b. p. 60–110°) m. p. 151–152° (cor.). In some experiments much better yields were obtained.

*Anal.* Calcd. for $C_{12}H_{12}O_2BrCl$: C, 47.44; H, 3.98; neut. equiv., 303.5. Found: C, 47.48; H, 4.06; neut. equiv., 304.

This compound was unchanged after sixty hours of irradiation in ethanol solution with a mercury arc lamp in a quartz flask.

**Resolution of *dl*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic Acid.**—To a solution of 8 g. of *dl*-β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic acid in 100 cc. of warm ethyl acetate was added 8.5 g. of quinine in 300 cc. of ethyl acetate. Upon cooling in an icebox, 6.78 g. of salt crystallized (fraction A) in white needles. After evaporation of the filtrate to 200 cc., 4.85 g. of salt (fraction B) crystallized. Further evaporation of the filtrate to 50 cc. gave 2.85 g. of salt as soft feathery needles.

Recrystallization of fraction A from ethyl acetate to constant rotation gave white needles, m. p. 184.5–186.5° with decomposition.

*Anal.* Calcd. for $C_{12}H_{12}O_2BrCl \cdot C_{20}H_{24}O_2N_2$: C, 61.19; H, 5.77; N, 4.46. Found: C, 61.73; H, 5.77; N, 4.53. *Rotation.* (*l*B*l*A salt) 0.0510 g. made up to 25 cc. in absolute ethanol at 20° gave $\alpha_D$ −0.43°; *l*, 2; $[\alpha]^{20}D$ −105°.

Two crystallizations of fraction C from ethyl acetate to which twice its volume of petroleum ether (b. p. 60–110°) had been added, gave soft feathery needles, m. p. 176.5–178° with decomposition.

*Rotation.* (*l*B*d*A salt) 0.0505 g. made up to 25 cc. in absolute ethanol at 20° gave $\alpha_D$ −0.24°; *l*, 2; $[\alpha]^{20}D$ −59.4°.

***d*- and *l*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic Acid.**—The decomposition of the salt was carried out in the same way as for the α-methylacrylic acid derivatives.[2]

The acids were recrystallized by dissolving in absolute ether, adding a third of its volume of petroleum ether (b. p. 60–110°) and allowing the solvent to evaporate slowly. Several crystallizations in this way did not change the rotation.

The *l*-acid was obtained as white needles, m. p. 161–163° (cor.), the *d*-acid, m. p. 158.5–159.5° (cor.); the latter obviously was not entirely pure.

*Anal.* Calcd. for $C_{12}H_{12}O_2BrCl$: C, 47.44; H, 3.98. Found: (*l*-acid) C, 47.63; H, 4.04.

*Rotation.* (*l*-acid) 0.0494 g. made up to 25 cc. with absolute ethanol at 20° gave $\alpha_D$ −0.28°; *l*, 2; $[\alpha]^{20}D$ −70.8°. (*d*-acid) 0.0502 g. made up to 25 cc. with absolute ethanol at 20° gave $\alpha_D$ +0.22°; *l*, 2; $[\alpha]^{20}D$ +54.2°.

**Racemization of *l*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic Acid.**—In boiling ethanol, no change in rotation occurred in ten hours.

In boiling *n*-butanol the readings were as follows:

*Rotation.* 0.0884 g. made up to 25 cc. with *n*-butanol at 25° gave $\alpha_D$ −0.48°; *l*, 2; $[\alpha]^{25}D$ −68°; after one hour, $\alpha_D$ −0.39°; two hours, $\alpha_D$ −0.31°; three hours, $\alpha_D$ −0.25°; four hours, $\alpha_D$ −0.20°; five hours, $\alpha_D$ −0.16°. Calculated for a reversible unimolecular reaction, half-life was 196 minutes. Repetition of this experiment which is necessarily qualitative because of the cooling necessary when readings were taken, half-life, 206 minutes.

**β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl)-N-acrylyl Glycine (VI).**—A mixture of 7 g. of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic acid and 5 g. of phosphorus pentachloride in a 25-cc. flask was warmed to 80°. The reaction proceeded without further application of heat. After thirty minutes, the phosphorous oxychloride was distilled at 1 mm. pressure (bath at 100°). The remaining oil was poured into a solution of 10 g. of glycine in 20 cc. of water. A 10% solution of sodium hydroxide was added slowly with shaking until the solution became basic to litmus. The mixture was poured into iced hydrochloric acid, whereupon a white solid precipitated. This was purified by crystallization from toluene: white silky crystals, m. p. 186–187° (cor.); yield, 4.8 g. (57.5%).

*Anal.* Calcd. for $C_{14}H_{15}O_3NBrCl$: C, 46.61; H, 4.19 Found: C, 47.08; H, 4.40.

**Resolution of *dl*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-N-acrylyl Glycine.**—A solution of 4.08 g. of the *dl*-acid in 150 cc. of ethyl acetate was added to 3.66 g. of quinine in 150 cc. of ethyl acetate. On evaporation to 200 cc. a total of 3.5 g. of salt crystallized. Recrystallization gave 2.2 g. of salt with no change in rotation; white plates, m. p. 123–125° (cor.).

*Anal.* Calcd. for $C_{14}H_{15}O_3NBrCl \cdot C_{20}H_{24}O_2N_2$: C, 59.60; H, 5.74. Found: C, 59.51; H, 6.10.

*Rotation.* (*l*A*l*B salt) 0.0502 g. made up to 10 cc. in absolute ethanol at 28° gave $\alpha_D$ −0.545°; *l*, 1; $[\alpha]^{28}D$ −108.5°.

***l* - β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl)-N-acrylyl Glycine.**—A suspension of 2.2 g. of the quinine salt in 20 cc. of concentrated hydrochloric acid was allowed to stand twelve hours. The solid was filtered, washed with water, dried and crystallized from toluene; white silky crystals, m. p. 185–186° (cor.).

*Anal.* Calcd. for $C_{14}H_{15}O_3NBrCl$: C, 46.61; H, 4.19. Found: C, 47.06; H, 4.21.

*Rotation.* (*l*-acid) 0.0500 g. made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ −0.26°; *l*, 2; $[\alpha]^{28}D$ −65.0°.

***d* - β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl)-N-acrylyl Glycine.**—The solution of the quinine salt from which the less soluble fractions had already been removed was reduced in volume to 50 cc. and cooled to 5°. About 2.8 g. of salt precipitated. This was dissolved in 50 cc. of warm ethyl acetate; upon cooling 1.9 g. of salt precipitated and was discarded. The remaining solution was reduced in volume to 25 cc. and cooled again to 5°. The 0.5 g. of salt that precipitated was suspended in 20 cc. of concentrated hydrochloric acid overnight. The solid was filtered, washed with water, dried and purified by crystallization from toluene: white silky needles, m. p. 185–186° (cor.).

*Anal.* Calcd. for $C_{14}H_{15}O_3NBrCl$: C, 46.61; H, 4.19. Found: C, 46.83; H, 4.32.

*Rotation.* (*d*-acid) 0.0440 g. made up to 25 cc. with absolute ethanol at 25° gave $\alpha_D$ +0.21°; *l*, 2; $[\alpha]^{28}D$ +59.7°.

**Racemization of *l*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-N-acrylyl Glycine.**—0.1100 g. of acid made up to 25 cc. with *n*-butanol at 28° gave $\alpha_D$ −0.55°; *l*, 2; $[\alpha]^{28}D$ −50°; after one hour, $\alpha_D$ −0.40°; two hours, $\alpha_D$ −0.29°; three hours, $\alpha_D$ −0.21°; four hours, $\alpha_D$ −0.16°; five hours, $\alpha_D$ −0.11°. The average half-life calculated

from these values was 128 minutes. Repetition of this experiment gave an average half-life of 138 minutes which checks the first half-life within the experimental error.

**Hydrolysis of *dl*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-N-acrylyl Glycine.**—To 0.5 g. of the glycine in 25 cc. of concentrated hydrochloric acid was added enough dioxane to make the mixture homogeneous. After seven hours of refluxing, the reddish-brown solution was poured into water. The oil which precipitated, solidified. After filtering and drying, the solid was extracted with petroleum ether (b. p. 60–110°). From the solvent a white solid precipitated which on recrystallization from the same solvent had a m. p. of 149.5–150.5° (cor.). A mixed m. p. with β-chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl) - acrylic acid showed no depression.

**2,4,6-Triethyl-3-bromoacetophenone.**—From 120.5 g. of 2,4,6-triethylbromobenzene in 300 cc. of carbon disulfide, 140 g. of anhydrous aluminum chloride and 51 g. of acetic anhydride was obtained 95 g. (67%) of product; colorless liquid, b. p. 125–127° (1 mm.); $n^{20}D$ 1.5431; $d^{20}_{20}$ 1.2596.

*Anal.* Calcd. for $C_{14}H_{19}OBr$: C, 59.36; H, 6.71. Found: C, 59.26; H, 6.72.

**2,4,6-Triethyl-3-bromobenzoylacetic Acid.**—From 25 g. of 2,4,6-triethyl-3-bromoacetophenone was obtained 16 g. of 2,4,6-triethyl-3-bromobenzoylacetic acid: white crystals from benzene, m. p. 107–109° (cor.) with decomposition. The crude compound was used for conversion to the chloroacrylic acid. This benzoylacetic acid decomposes on standing.

**β - Chloro - β - (2,4,6 - triethyl - 3 - bromophenyl) - acrylic Acid (IV).**—From 10 g. of 2,4,6-triethyl-3-bromobenzoylacetic acid was obtained 8 g. (76%) of β-chloro-β-(2,4,6-triethyl-3-bromophenyl)-acrylic acid: white crystals from petroleum ether (b. p. 60–110°), m. p. 115–116° (cor.).

*Anal.* Calcd. for $C_{15}H_{12}O_2ClBr$: C, 52.10; H, 5.21. Found: C, 52.21; H, 5.47.

In spite of all attempts with a variety of alkaloids, no crystalline salts for resolution could be found. As a consequence, the acid was converted to the glycine.

**β - Chloro - β - (2,4,6 - triethyl - 3 - bromophenyl) - N-acrylyl Glycine (V).**—A mixture of 5.9 g. of β-chloro-β-(2,4,6-triethyl-3-bromophenyl)-acrylic acid and 4.2 g. of phosphorus pentachloride was heated to 100° for fifteen minutes. The resulting phosphorus oxychloride was distilled at 1 mm. pressure and the residual oil poured into a solution of 10 g. of glycine in 20 cc. of water. To this mixture was added drop by drop a 10% aqueous solution of sodium hydroxide until it reacted basic to litmus. After shaking for fifteen minutes, it was poured into iced hydrochloric acid. The product was extracted with petroleum ether (b. p. 60–110°) to remove traces of the original acid and then was crystallized from toluene: white silky crystals, m. p. 185–186° (cor.); yield 6.8 g. (99%).

*Anal.* Calcd. for $C_{17}H_{21}O_3NBrCl$: C, 50.67; H, 5.25; neut. equiv., 408. Found: C, 50.41; H, 5.36; neut. equiv., 403.

**Resolution of β-Chloro-β-(2,4,6-triethyl-3-bromophenyl)-N-acrylyl Glycine.**—To 6 g. of β-chloro-β-(2,4,6-triethyl-3-bromophenyl)-N-acrylyl glycine in 50 cc. of warm absolute ethanol was added 4.85 g. of quinine in 50 cc. of the same solvent. The solution was cooled and salt filtered, the filtrate was evaporated somewhat, again cooled and salt filtered. This was repeated a third time. Each fraction thus isolated gave the same rotation; all three fractions amounted to 5 g. Recrystallization of the combined fractions from absolute ethanol gave 3.4 g. of salt of the same rotation.

The remainder of the original solution after separation of 5 g. of the less soluble salt was evaporated to dryness and extracted with three 100-cc. portions of hot ethyl acetate. Both salts are much less soluble in ethyl acetate than in ethanol, the less soluble in ethanol being practically insoluble in cold ethyl acetate. The ethyl acetate extracts were cooled and the salt that crystallized was filtered and discarded. Fractions of salt were isolated by gradual evaporation until successive fractions gave a constant rotation. Evaporation to dryness gave additional salt. The product melted at 222–223° (cor.) with decomposition.

*Anal.* Calcd. for $C_{17}H_{21}O_3NBrCl \cdot C_{20}H_{24}O_2N_2$ (*l*B*l*A): C, 61.07; H, 6.24. Found: C, 61.41; H, 6.33.

*Rotation.* (less soluble salt (*l*B*l*A)) 0.0500 g. made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ −0.46°; *l*, 2; $[\alpha]^{28}D$ −115°. (more soluble salt (*l*B*d*A)) 0.0501 g. made up to 25 cc. in absolute ethanol at 28° gave $\alpha_D$ −0.25°; *l*, 2; $[\alpha]^{28}D$ −62.5°. Neither salt showed any signs of mutarotation.

***d*- and *l*-β-Chloro-β-(2,4,6-triethyl-3-bromophenyl)-N-acrylyl Glycine.**—The salts were decomposed by suspending in concentrated hydrochloric acid for eight to ten hours. The active acids were crystallized from toluene; white crystals, m. p. 185–186° (cor.).

*Anal.* Calcd. for (*l*-acid or *d*-acid): C, 50.67; H, 5.25. Found: (*l*-acid) C, 50.61; H, 5.28; (*d*-acid) C, 51.06; H, 5.46.

*Rotation.* (*l*-acid) 0.0501 g. made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ −0.20°; *l*, 2; $[\alpha]^{28}D$ −49.9°. (*d*-acid) 0.0500 g. made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ +0.20°; *l*, 2; $[\alpha]^{28}D$ +50.0°. These acids did not racemize upon boiling for twelve hours in *n*-butanol.

**2,4,6-Triethyl-3-bromopropiophenone.**—Colorless oil, b. p. 127–129° (1 mm.); yield 66%.

*Anal.* Calcd. for $C_{15}H_{21}OBr$: C, 60.61; H, 7.07. Found: C, 60.33; H, 6.69.

**α - Methyl - (2,4,6 - triethyl - 3 - bromobenzoyl) - acetic Acid.**—White crystals from benzene, m. p. 113–115° (cor.) with decomposition; yield 57%.

*Anal.* Calcd. for $C_{16}H_{21}O_3Br$: C, 56.30; H, 6.16. Found: C, 56.58; H, 6.11.

**β - Chloro - β - (2,4,6 - triethyl - 3 - bromophenyl) - α - methylacrylic Acid (III).**—White crystals, m. p. 146–148° (cor.); yield 80%.

*Anal.* Calcd. for $C_{16}H_{20}O_2BrCl$: C, 53.43; H, 5.56. Found: C, 53.38; H, 5.71.

**Resolution of *dl*-β-Chloro-β-(2,4,6-triethyl-3-bromophenyl)-α-methylacrylic Acid.**—A mixture of 8.99 g. of *dl*-acid in 50 cc. of methanol and 11.65 g. of brucine in 50 cc. of methanol on standing deposited 11.7 g. of salt. This salt was recrystallized slowly five times from methanol with a slow change in rotation after each recrystallization. The

change was in the range of experimental error on the last fraction. About 4 g. of salt was thus obtained as white crystals, m. p. 107–110° (cor.) with decomposition.

*Anal.* Calcd. for $C_{16}H_{20}O_2BrCl \cdot C_{23}H_{26}O_4N_2 \cdot CH_3OH$: C, 61.09; H, 6.41. Found: C, 61.24; H, 6.23.

*Rotation.* (*l*BdA) 0.0999 g. made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ −0.11°; *l*, 2; $[\alpha]^{28}D$ −13.8°.

**d - β - Chloro - β - (2,4,6 - triethyl - 3 - bromophenyl) - α-methylacrylic Acid.**—The salt was decomposed by washing five times with dilute hydrochloric acid. The remaining solid was washed with water, dried, and crystallized from petroleum ether (b. p. 60–110°); yield 1.6 g. of acid, 0.1 g. of which in 25 cc. of ethanol had an observed rotation of +0.01°. Obviously, only a very small separation had been effected by the recrystallization of the brucine salt. The 1.8 g. of acid was fractionally crystallized six times from petroleum ether (b. p. 60–110°). It was found that the racemic form was much less soluble than the active form. By this procedure a small amount of acid was obtained with a fairly high rotation; white crystals, m. p. 146–148° (cor.).

*Anal.* Calcd. for $C_{16}H_{20}O_2BrCl$: C, 53.43; H, 5.56. Found: C, 53.63; H, 5.57.

*Rotation.* 0.0999 g. of acid made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ +28°; *l*, 2; $[\alpha]^{28}D$ +35.0°.

Decomposition of the more soluble salt fraction gave an acid with no apparent rotation. Repeated crystallization gave an acid with a slight rotation.

*Rotation.* 0.1002 g. of acid made up to 25 cc. with absolute ethanol at 28° gave $\alpha_D$ −0.03°; *l*, 2; $[\alpha]^{28}D$ −3.74°.

The *d*-acid did not racemize by boiling in *n*-butanol solution for ten hours.

**β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl) - α-methyl-N-acrylyl Glycine (VII).**—A mixture of 10 g. of β - chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl) - α-methylacrylic acid and 10 g. of phosphorus pentachloride was kept at 75° for ten minutes. The phosphorus oxychloride was distilled off under reduced pressure and the residual oil was poured into a solution of 20 g. of ethyl glycinate in 50 cc. of benzene. This mixture was refluxed for thirty minutes. After evaporation of the benzene, the residue was dissolved in 100 cc. of dioxane and 25 cc. of 37% hydrochloric acid and heated under reflux for thirty minutes. The dioxane solution was diluted with water, extracted with benzene and the benzene in turn extracted with 5% aqueous sodium hydroxide. Acidification of the alkaline solution gave 7.1 g. (60%) of a white solid. Several recrystallizations from benzene gave pure white crystals, m. p. 179–180° (cor.).

*Anal.* Calcd. for $C_{15}H_{17}O_3NClBr$: C, 48.10; H, 4.57. Found: C, 48.45; H, 4.70.

**l - β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl) - α-methyl-N-acrylyl Glycine.**—A hot solution of 6.8 g. of β - chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl) - α-methyl-N-acrylyl glycine and 5.9 g. of quinine in 100 cc. of a hot 50% methanol–water mixture was allowed to cool. About 3.5 g. of a crystalline salt precipitated. Three recrystallizations from 50% methanol–water gave 1.1 g. of salt whose rotation did not change with further recrystallization; m. p. 121.5–122.5° (cor.).

*Anal.* Calcd. for $C_{15}H_{17}O_3NClBr \cdot C_{20}H_{24}O_2N_2$: N, 6.01. Found: N, 5.92.

*Rotation.* 0.0503 g. made up to 25 cc. with methanol at 26° gave $\alpha_D$ −0.52°; *l*, 2; $[\alpha]^{26}D$ −129°.

The salt was decomposed with cold 20% hydrochloric acid. The active acid was recrystallized from benzene, m. p. 179–180° (cor.).

*Anal.* Calcd. for $C_{15}H_{17}O_3NClBr$ (*l*-form): C, 48.10; H, 4.57. Found: C, 48.50; H, 4.76.

*Rotation.* 0.0503 g. made up to 25 cc. with *n*-butanol at 26° gave $\alpha_D$ −0.285°; *l*, 2; $[\alpha]^{26}D$ −70.9°.

The rotation remained unchanged after refluxing a solution of the compound in *n*-butanol for ten hours.

## Summary

1. β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl)-acrylic acid has been prepared and resolved. The active compound racemized in boiling butanol with a half-life of 200 minutes, whereas *l*-β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid was stable under these conditions.

2. Both β-chloro-β-(2,4,6-triethyl-3-bromophenyl)-acrylic acid and the corresponding α-methylacrylic acid were synthesized. The latter was resolved and did not racemize in boiling butanol. The former did not give crystalline salts suitable for resolution so was converted into the glycine by forming the acid chloride and condensing with glycine. This product was resolved and the active forms did not racemize in boiling butanol.

3. The glycine of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid was resolved and the active forms proved to be resistant to racemization.

4. β - Chloro - β - (2,4,6 - trimethyl - 3 - bromophenyl)-N-acrylyl glycine was made and resolved. The active acid was less stable (half-life 133 minutes) than the active β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-acrylic acid. A discussion is given of the possible reasons for this peculiar result.

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