TABLE I

PROPERTIES OF FURAN DERIVATIVES, R = FURAN

R	B. p., °C.	Mm.	Yield, %[a]	Hydrochloride M. p., °C.	Formula	Composition, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
2-(1-Oxo-2-piperidinoethyl)	139–140	4	73	264–266[b]	$C_{11}H_{16}ClNO_2$	57.51	57.43	7.02	7.32
2-(1-Hydroxy-2-piperidinoethyl)	127–128	5	38	172–174	$C_{11}H_{18}ClNO_2$	57.01	56.73	7.83	8.15
2-(1-Hydroxy-2-piperidinoethyl)-tetrahydro	125–126	4	64	170–173[c]	$C_{11}H_{22}ClNO_2$	56.04	55.79	9.41	9.69
2-(1-Acetoxy-2-piperidinoethyl)-tetrahydro	.....	..	..	191–194	$C_{13}H_{24}ClNO_3$	...	...	5.04[d]	5.37[d]
2-(1-Oxo-2-morpholinoethyl)	.....	..	49	221–229[b]	$C_{10}H_{14}ClNO_3$	51.84	51.86	6.09	6.58
2-(1-Hydroxy-2-morpholinoethyl)	146–150	5[e]	70[f]	185–186[b]	$C_{10}H_{16}ClNO_3$	51.39	51.59	6.90	7.20[g]
2-(1-Acetoxy-2-morpholinoethyl)	.....	..	..	166–167[b]	$C_{12}H_{18}ClNO_4$	52.27	52.48	6.58	6.62
2-(1-Hydroxy-2-morpholinoethyl)-tetrahydro[h]	138–140	12	41	170–176	$C_{10}H_{20}ClNO_3$	50.52	51.57	8.48	7.86
2-[1-Oxo-2-(4-methylpiperidino)-ethyl]	133–139	4	51	253–265	$C_{12}H_{18}ClNO_2$	59.13	59.01	7.44	7.69
2-[1-Hydroxy-2-(4-methylpiperidino)-ethyl]	126–128	4	74[f]	70–72[f]	$C_{12}H_{19}NO_2$[f]	68.86	68.76[f]	9.15	9.45[f]
2-[1-Acetoxy-2-(4-methylpiperidino)-ethyl]	.....	..	..	179–181[b]	$C_{14}H_{22}ClNO_3$	...	...	4.86[d]	4.96[d]
2-[1-Hydroxy-2-(4-methylpiperidino)-ethyl]-tetrahydro	131–132	4	33[f]	.....	$C_{12}H_{23}NO_2$[f]	...	...	6.57[d]	6.78[d,f]
3-(1-Keto-3-dimethylaminopropyl)-2,5-dimethyl[i]	.....	..	..	175–177	$C_{11}H_{18}ClNO_2$	...	...	6.04[d]	5.97[d]

[a] Yields of hydrochloride are reported, whenever oily bases were converted to hydrochloride for purification. [b] With decomposition. [c] Mixed melting point with hydrochloride just above showed a 20° depression. [d] Nitrogen analysis. [e] M. p., 67–68°; purified by sublimation at 70° (1 mm.). [f] Free base. [g] Nitrogen analysis on free base: calcd., 7.10; found, 7.09. [h] Hydrochloride hygroscopic. [i] Prepared by the Mannich reaction from 2,5-dimethyl-3-acetylfuran, paraformaldehyde and dimethylamine hydrochloride. Recrystallized from ethanol–ether.

ten to twelve hours. The catalyst was filtered off, the solvent evaporated under reduced pressure, the bases were liberated with alkali and extracted into ether. The tetrahydrofuryl amino alcohols (IV) were purified by fractional distillation. They appeared as colorless oils and were submitted for pharmacological tests except in those cases in which crystalline salts could be prepared.

Acetyl Derivatives.—Acetylation of the furyl and tetrahydrofuryl amino alcohols was carried out by heating the free bases with an excess of acetic anhydride at 100° for one hour. The hydrochlorides usually crystallized when ethereal hydrogen chloride was added to the reaction mixture.

Summary

Tetrahydrofuran derivatives containing tertiary α-amino alcohol groups in position-2 were prepared in a systematic study of potential analgesics.

2-(1-Oxo-2-dialkylaminoethyl)-furans were reduced to the corresponding amino alcohols with aluminum isopropoxide, and nuclear hydrogenation was accomplished by use of Raney nickel catalyst at ordinary pressure.

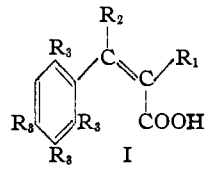
CHARLOTTESVILLE, VA. RECEIVED JULY 28, 1943

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

Restricted Rotation in Aryl Olefins. VIII. The Synthesis and Resolution of Certain β-Substituted-β-arylacrylic Acids

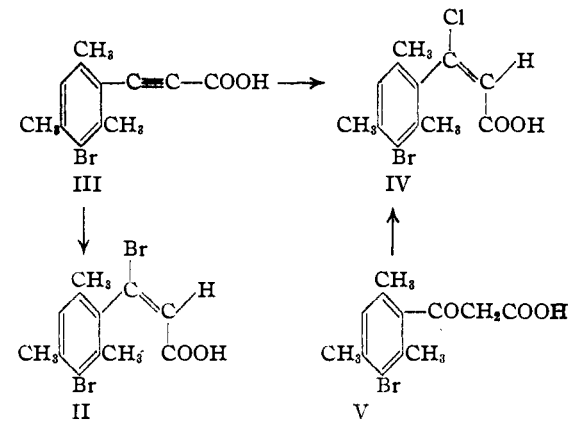
BY ROGER ADAMS AND C. W. THEOBALD[1]

A comparison of the effect of varying the R_2 group upon the rate of racemization of hindered acrylic acid molecules of Type I has not been made previously. This has now been undertaken, since a feasible method of synthesis for such molecules has been devised.[2]



I

β-Bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid (II), made by addition of hydrogen bromide to 3-bromo-2,4,6-trimethylphenylpropiolic acid (III), was resolved and the rate of racemization determined and compared with that of β-chloro-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid (IV)[3] synthesized by the action of phosphorus pentachloride on 3-bromo-2,4,6-trimethylbenzoylacetic acid (V) or by the addition



III IV

II V

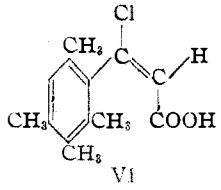
(1) An abstract of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry: Eastman Kodak Fellow, 1942–43.

(2) Adams and Theobald, THIS JOURNAL, **65**, 2208 (1943).

(3) Adams, Anderson and Miller, *ibid.*, **63**, 1589 (1941).

of hydrogen chloride to 3-bromo-2,4,6-trimethylphenylpropiolic acid (III). Compound IV had a half-life of two hundred minutes in boiling *n*-butanol while compound II under similar conditions had a half-life of sixty-four hours. It is thus obvious that change of the β-substituent has a marked influence on the restricted rotation and that the bromine atom is much more influential in inducing restricted rotation than the chlorine atom. This relative effect of bromine and chlorine has been observed in the biphenyl series.[4]

β-Chloro-β-(2,3,4,6-tetramethylphenyl)-acrylic acid[2] (VI) was prepared by addition of hydrogen chloride to 2,3,4,6-tetramethylphenylpropiolic acid or by the action of phosphorus pentachloride on 2,3,4,6-tetramethylbenzoylacetic acid. The active form gave a half-life of one hundred and seventy-four minutes This rate is not significantly different from that (200 minutes) of compound IV, thus indicating the relatively minor change in stability of the molecule effected by replacing a bromine atom by a methyl group in the 3-position of the benzene ring.

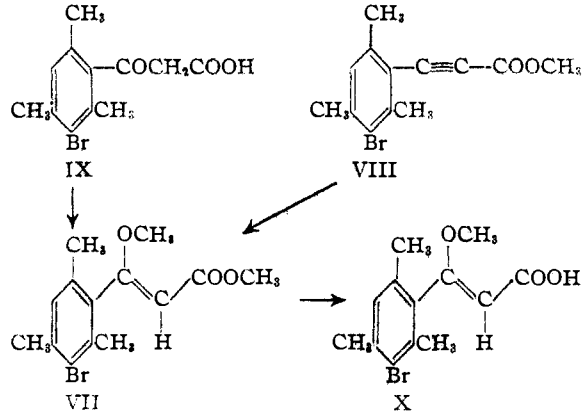


VI

Since the same chloroacrylic acid results from addition of hydrogen chloride to an arylpropiolic acid or by the action of phosphorus pentachloride on the corresponding benzoylacetic acid as demonstrated in the mesityl and isoduryl derivatives, it was assumed that addition of hydrogen bromide to an arylpropiolic acid would give a similar configuration. Thus it may be deduced that compounds II and IV each have the halogen and carboxyl group *trans* to each other.

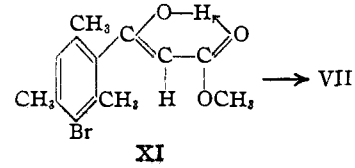
This configuration of the halogen and carboxyl groups with respect to each other and to the ring has been assumed on the basis of facts discussed in previous papers.[3,5]

Methyl β-methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylate (VII) was prepared in two ways, (1) addition of sodium methylate to methyl 3-bromo-2,4,6-trimethylphenylpropiolate (VIII) or by the action of diazomethane on 3-bromo-2,4,6-trimethylbenzoylacetic acid (IX). By alkaline saponification of the ester, β-methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid (X) resulted. This acid (X) formed well-crystallized salts with brucine and quinine but the salts were not mutarotating and no resolution was effected. This unexpected result can best be explained on the assumption that the relative positions of the hydrogen and carboxyl groups in the molecule probably are different from those in compound II or IV in that the carboxyl group is *cis* to the methoxyl. Under these conditions, non-resolution of compound X might be anticipated from a study of the models, whereas a molecule with the methoxyl and carboxyl groups *trans* to each other and the carboxyl group *cis* to the ring should be resolvable, though the active forms might be racemized easily.



IX VIII VII X

The formation of compound VII from the aroylacetic acid (IX) and diazomethane proceeds through the ester which undoubtedly would chelate in the stable enol form (XI). Upon further methylation, the configuration would be maintained in the β-methoxy ester (VII) and in the acid (X) after saponification. On the assumption



XI

that the structure postulated for compound VII is correct, sodium methylate must add *trans* to the triple bond of the arylpropiolic acid in order that an acid of the same structure as that from diazomethane and the aroylacetic acid would be formed.

The synthesis of α-chloro-α-(3-bromo-2,4,6-trimethylphenyl)-ethylene deserves mention since the published procedure[6] for synthesizing this type of compound failed to give other than a very impure product. It was found that, under the conditions previously described, ω-chloroacetobromomesitylene was formed in appreciable amounts during the conversion of the acetobromomesitylene to α-chloro-α-(3-bromo-2,4,6-trimethylphenyl)-ethylene and could not be removed readily. By conducting the reaction at a low temperature in the presence of phosphorus trichloride pure α-chloro-α-(3-bromo-2,4,6-trimethylphenyl)-ethylene could be obtained. Dehydrohalogenation of this substance to bromomesitylacetylene could not be accomplished satisfactorily either with sodium amide in xylene or by aqueous ethanolic alkali. Sodium ethylate in absolute ethanol was selected as the reagent and a pure product isolated.

(4) Stoughton and Adams, THIS JOURNAL, **54**, 4426 (1932).

(5) Adams and Gross, *ibid.*, **64**, 1786 (1942).

(6) Vaughn and Nieuwland, *ibid.*, **56**, 1207 (1934).

Experimental

Acetobromomesitylene.—The directions previously described[7] gave a poor yield of the desired ketone when applied to a large scale preparation owing to an excessive amount of rearrangement to tribromomesitylene. This troublesome factor was eliminated by using the following procedure. A solution of 500 g. (2.5 moles) of bromomesitylene in 265 g. (2.6 moles) of acetic anhydride was dropped into a stirred suspension of 700 g. (5.2 moles) of aluminum chloride in 1200 cc. of carbon disulfide at such a rate that gentle refluxing occurred. Stirring and refluxing on a steam cone were continued for two hours after complete addition of the acetic anhydride solution. The reaction mixture was decomposed by pouring onto iced hydrochloric acid. The aqueous layer was decanted and extracted with ether. The carbon disulfide and ether were removed by distillation and the residue taken up in ether and washed with water, dilute aqueous hydrochloric acid, water, dilute aqueous sodium carbonate and finally with water. Distillation of the dried ether layer and redistillation of the main fraction gave a colorless liquid which became yellow on standing; b. p. 121° (4 mm.); $n^{20}D$ 1.5551; yield 445 g. (74%).

2,4,6-Trimethyl-3-bromo-5-nitroacetophenone.—A 1-cc. portion of acetobromomesitylene was dropped slowly into 10 cc. of ice-cold fuming nitric acid (sp. gr. 1.50). After five minutes the mixture was diluted with ice-water and the nitrated derivative purified by recrystallization from petroleum ether (b. p. 90–110°) or from ethanol; pale yellow cubes m. p. 119–120° (cor.).

Anal. Calcd. for $C_{11}H_{12}O_3NBr$: C, 46.17; H, 4.23. Found: C, 46.59; H, 4.32.

α-Chloro-α-(3-bromo-2,4,6-trimethylphenyl)-ethylene.—A solution of 210 g. of acetobromomesitylene in 250 cc. of phosphorus oxychloride and 75 cc. of phosphorus trichloride was treated with 185 g. of phosphorus pentachloride and heated to 65° for seventeen hours, then to 90° for one hour longer.[2] The product was isolated in the usual manner and purified by distillation, yielding the following fractions: (1) b. p. 105–114° (0.3 mm.); weight 130 g.; (2) b. p. 114–130° (0.3 mm.); weight 15 g.; (3) b. p. 131–140° (0.3 mm.); weight 27 g.; (4) residue not distilling below 150° (0.3 mm.). Fractions 1 and 2 were redistilled separately yielding a water-white liquid; b. p. 109–110° (0.3 mm.), $n^{20}D$ 1.5690, d^{20} 1.3977; yield 135 g. (63%).

Anal. Calcd. for $C_{11}H_{12}BrCl$: C, 50.89; H, 4.66. Found: C, 50.87; H, 4.68.

The material in fraction 3, b. p. 131–140° (0.3 mm.) solidified and was purified by recrystallization from petroleum ether (b. p. 90–110°); clusters of white needles, m. p. 64–65° (cor.); yield 27 g. (11.5%). This compound was ω-chloroacetobromomesitylene.

Anal. Calcd. for $C_{11}H_{12}OBrCl$: C, 47.94; H, 4.39. Found: C, 47.57; H, 4.50.

The alkaline washings of the ether extracts were acidified, precipitating an oil which crystallized slowly. The oily material was removed by extraction with boiling carbon tetrachloride and the residue recrystallized from aqueous methanol; m. p. 209–212° (cor.); yield 23 g. (8.5%). The analytical data indicated that this acid was a phosphoric acid ester of α-hydroxy-α-(3-bromo-2,4,6-trimethyl)-ethylene. However, the analytical data were not consistent.

3-Bromo-2,4,6-trimethylphenylacetylene.—A solution of 110 g. of α-chloro-α-(3-bromo-2,4,6-trimethylphenyl)-ethylene in 50 cc. of absolute ethanol was added dropwise to a stirred solution of sodium ethylate, prepared by adding 19.5 g. of sodium to 300 cc. of absolute ethanol. Refluxing and stirring were continued (bath temperature 110°) for six hours, then 150 cc. of ethanol was removed by distillation and the residue poured into dilute iced hydrochloric acid. The product was removed by extraction with ether and washed with water, 10% aqueous sodium carbonate, and water and dried over Drierite. Distillation gave the following fractions: (1) b. p. 92–95° (0.3 mm.); weight 39 g.; (2) b. p. 95–100° (0.3 mm.), weight 28 g.; (3) b. p. above 100° (0.3 mm.); weight 6 g.; (4) polymeric residue; 13 g. Redistillation of fractions 1 and 2 yielded a water-white liquid which turned purple on standing; b. p. 84° (0.2 mm.), $n^{20}D$ 1.5871, d^{20} 1.3159; yield 54 g. (57%).

Anal. Calcd. for $C_{11}H_{11}Br$: C, 59.21; H, 4.97. Found: C, 59.23; H, 5.11.

The *bis*-mercuri derivative melted at 255° (cor.).[8]

3-Bromo-2,4,6-trimethylphenylpropiolic Acid.—This acid was prepared by the general procedure used for the synthesis of 2,4,6-trimethylphenylpropiolic acid.[2] From 18.5 g. of 3-bromo-2,4,6-trimethylphenylpropiolic acid and a solution of ethylmagnesium bromide prepared from 3.5 g. of magnesium and 18 g. of ethyl bromide, was obtained 15.5 g. of crude acid. Recrystallization from benzene, petroleum ether (b. p. 90–110°) or aqueous ethanol gave long white needles; m. p. 168–169° (cor.); yield 14 g. (63%).

Anal. Calcd. for $C_{12}H_{11}O_2Br$: C, 53.95; H, 4.15. Found: C, 54.06; H, 4.25.

The same acid was obtained in 75% yield from β-chloro-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid heated for one hour with 10% aqueous sodium hydroxide. The propiolic acid prepared in this way was difficult to purify completely, varying in color from light tan to purple.

β-Chloro-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acid.—The addition of hydrogen chloride to 3-bromo-2,4,6-trimethylphenylpropiolic acid in glacial acetic acid according to a previously described procedure[2] resulted in a yield of 86% of chloroacrylic acid which was identical in melting point and gave no depression of a mixed melting point with a sample of this acid prepared by Adams, Anderson and Miller[3] from 3-bromo-2,4,6-trimethylbenzoylacetic acid and phosphorus pentachloride.

β-Bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acid.—Dry hydrogen bromide was bubbled for eight hours through a solution of 13 g. of 3-bromo-2,4,6-trimethylphenylpropiolic acid in 200 cc. of glacial acetic acid maintained at 65–70°. The product was isolated by pouring the acetic acid solution into 500 cc. of ice-water, and purified by recrystallization from petroleum ether (b. p. 90–110°) and from aqueous ethanol; white crystals m. p. 158.5–159.5° (cor.); yield 14 g. (83%).

Anal. Calcd. for $C_{12}H_{12}O_2Br_2$: C, 41.41; H, 3.47. Found: C, 41.73; H, 3.62.

3-Bromo-2,4,6-trimethylbenzoylacetic Acid.—The compound as previously prepared was reported as having a melting point of 98–99°.[2] Following the same procedure there was obtained a 68% yield of an acid, m. p. 114–115° (cor.) with decomposition. This acid decarboxylated to acetobromomesitylene.

Anal. Calcd. for $C_{12}H_{13}O_3Br$: C, 50.52; H, 4.56. Found: C, 50.84; H, 4.73.

Methyl 3-Bromo-2,4,6-trimethylphenylpropiolate.—The acetylenic Grignard was prepared by adding 22.3 g. of 3-bromo-2,4,6-trimethylphenylacetylene in 60 cc. of anhydrous ether to a solution of ethylmagnesium bromide prepared from 3.6 g. of magnesium and 16.4 g. of ethyl bromide in 60 cc. of ether. The resulting solution was refluxed for two hours and dropped slowly into a stirred solution of 15.6 g. of methyl chlorocarbonate in 120 cc. of anhydrous ether. Refluxing and stirring were continued for twelve hours after the addition, then a solution of 15 cc. of concentrated hydrochloric acid in 100 cc. of water was added dropwise to decompose the reaction mixture. The ether layer was washed with water, 10% aqueous sodium carbonate and water, then dried with anhydrous sodium sulfate and concentrated under a gentle air stream. The oily residue was extracted several times with 50-cc. portions of boiling methanol. The ester was isolated by evaporation of methanol solution and recrystallized from methanol; white plates, m. p. 83.5–85° (cor.); yield, 14.5 g. (52%).

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

(8) Johnson and McEwen, *ibid.*, **48**, 469 (1926).

Anal. Calcd. for $C_{13}H_{13}O_2Br$: C, 55.53; H, 4.66. Found: C, 55.78; H, 4.73.

The methanol insoluble oil crystallized when triturated with petroleum ether (b. p. 30–60°) and was recrystallized from ethyl acetate; yellow to orange powder, m. p. 160–161° (cor.); yield, 2 g. The structure of this compound was not determined.

Anal. Calcd. for $C_{13}H_{13}Br$: C, 62.67; H, 5.26; Br, 32.08. Found: C, 62.65, 62.55; H, 5.36, 5.45; Br, 32.33.

Methyl β-Methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylate.—The general procedure used was that described by Moureu.[9] A solution of one mole equivalent of sodium methylate in 3 cc. of absolute methanol was added to 2.23 g. of methyl 3-bromo-2,4,6-trimethylphenylpropiolate in 12 cc. of hot methanol and refluxed vigorously for twelve hours. The solvent was removed by distillation and iced hydrochloric acid was added to the residue. The product was extracted with ether and the ether removed leaving an oil which soon crystallized. The ester was recrystallized from petroleum ether (b. p. 90–110°); white cubes m. p. 78–79.5° (cor.); yield, 1.5 g. (60%).

Anal. Calcd. for $C_{14}H_{17}O_3Br$: C, 53.69; H, 5.47. Found: C, 53.46; H, 5.66.

An ester of the same melting point and mixed melting point was obtained by the action of diazomethane on 3-bromo-2,4,6-trimethylbenzoylacetic acid.[10]

β-Methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acid.—A solution of 4 g. of potassium hydroxide in 14 cc. of water was added to a solution of 8.57 g. of methyl β-methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylate in 40 cc. of ethanol and refluxed for ten hours. Most of the ethanol and methanol was removed under reduced pressure and to the residue was added 100 cc. of ice-water. The cold alkaline solution was extracted with ether and neutralized in the cold to the congo red end-point with ice-cold 5% aqueous sulfuric acid. The acid was removed rapidly, washed with water and recrystallized from methanol; white plates m. p. 156–157° (cor.) with decomposition; yield, 7.61 g. (93%).

Anal. Calcd. for $C_{13}H_{15}O_3Br$: C, 52.19; H, 5.05. Found: C, 52.25; H, 5.19.

Resolution of β-Bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acid.—A solution of 7 g. of β-bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid in 25 cc. of warm absolute ethanol was added to a solution of 6.524 g. of quinine in 50 cc. of absolute ethanol. The resulting solution was filtered, diluted to a total volume of 100 cc. of solvent, and cooled yielding 3.655 g. of salt (fraction A). Fractions B and C were removed after evaporation of the solvent to 40 cc. then 20 cc. and weighed 0.850 g. and 1.584 g., respectively. Fraction D (0.50 g.) was obtained by the addition of 20 cc. of petroleum ether (b. p. 30–60°) to the mother liquor from fraction C. Evaporation to dryness under reduced pressure yielded 5.860 g. of salt (fraction E)

Fraction A was twice recrystallized from absolute ethanol, after which a constant rotation had been reached; white plates m. p. 175° (cor.) with decomposition.

Anal. Calcd. for $C_{32}H_{36}N_2O_4Br_2$: C, 57.15; H, 5.40; N, 4.17. Found: C, 57.90; H, 5.81; N, 4.29.

Rotation. Less soluble salt (*l*B·*l*A) 0.0647 g. made up to 10 cc. with absolute ethano at 26° gave α_D −0.54; *l*, 1; $[\alpha]^{26}D$ −83.2°.

Fraction E was purified by three recrystallizations from a mixture of equal volumes of benzene and petroleum ether (b. p. 90–110°) with no change in rotation after the last crystallization; sandy white granules m. p. 164–164.5° (cor.) with decomposition.

Anal. Calcd. for $C_{32}H_{36}N_2O_4Br_2$: C, 57.15; H, 5.40; N, 4.17. Found: C, 57.50; H, 5.49; N, 4.20.

Rotation. More soluble salt (*l*B·*d*A) 0.0260 g. made up to 5 cc. with absolute ethanol at 28° gave α_D −0.25; *l*, 1; $[\alpha]^{28}D$ −48.1°.

d- and *l*-β-Bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acids.—The salts were decomposed by stirring with an excess of aqueous acid containing 10 cc. of concentrated hydrochloric acid to 100 cc. of water. Decomposition of 1.700 g. of purified fraction A yielded 0.840 g. of *l*-acid crystallizing in thick white needles from petroleum ether; m. p. 155–155.5° (cor.).

Anal. Calcd. for $C_{13}H_{12}O_2Br_2$: C, 41.41; H, 3.47. Found: C, 41.48; H, 3.69.

Rotation. (*l*-acid) 0.0605 g. made up to 10 cc. with absolute ethanol at 25° gave α_D −0.225; *l*, 1; $[\alpha]^{25}D$ −37.2°.

A 1.185-g. portion of the purified more soluble salt (fraction E) was similarly decomposed yielding 0.585 g. of *d*-acid. This *d*-acid was recrystallized three times from petroleum ether (b. p. 90–110°) with no change in rotation; m. p. 155–156° (cor.).

Rotation. (*d*-acid) 0.0298 g. made up to 5 cc. with absolute ethanol at 28° gave α_D +0.20; *l*, 1; $[\alpha]^{28}D$ +33.6°.

Racemization of *l*-β-bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acid.—0.3521 g. of *l*-acid made up to 15 cc. with *n*-butanol gave α_D −0.67; after twelve hours, α_D −0.59; twenty-four hours, α_D −0.519; thirty-six hours, α_D −0.45; forty-eight hours, α_D −0.39; sixty hours, α_D −0.34; eighty-four hours, α_D −0.264. The average half-life calculated from these figures assuming a reversible first order reaction was sixty-two and two-tenths hours. Repetition of this experiment gave half-lives of sixty-eight and one-half, and fifty-six and one-tenth hours.

Resolution of β-Chloro-β-(2,3,4,6-tetramethylphenyl)-acrylic Acid.[3]—A solution of 5 g. of β-chloro-β-(2,3,4,6-tetramethylphenyl)-acrylic acid in 50 cc. of hot ethyl acetate was added to a hot solution of 6.8 g. of quinine in 100 cc. of ethyl acetate and filtered. When cooled to room temperature this solution deposited 6.425 g. of salt (fraction 1) and an additional 0.160 g. when cooled to 0° (fraction 2). Fractions 3, 4, and 5 were removed at 75 cc., 35 cc. and by evaporation to dryness yielding 1.654 g., 1.272 g. and 2.158 g., respectively.

Fraction 1 was purified by recrystallization from ethyl acetate to which a small amount of ethanol had been added to increase the solubility of the salt. A constant rotation was reached after two crystallizations; large transparent cubes, m. p. 193–194° (cor.) with decomposition.

Anal. Calcd. for $C_{33}H_{39}N_2O_4Cl$: C, 70.38; H, 6.98; N, 4.98. Found: C, 70.79; H, 6.98; N, 5.06.

Rotation. Less soluble salt (*l*B·*l*A) 0.0530 g. made up to 10 cc. with absolute ethanol at 28° gave α_D −0.445; *l*, 1; $[\alpha]^{28}D$ −84.0°.

Fraction 4 was purified by recrystallization from benzene–petroleum ether (b. p. 90–110°); long white needles, m. p. 163–165° (cor.) with decomposition.

Anal. Calcd. for $C_{33}H_{39}N_2O_4Cl$: C, 70.38; H, 6.98; N, 4.98. Found: C, 70.64; H, 7.15; N, 5.10.

Rotation. More soluble salt (*l*B·*d*A) 0.0508 g. made up to 10 cc. with absolute ethanol at 28° gave α_D −0.303; *l*, 1; $[\alpha]^{28}D$ −59.6°.

d- and *l*-β-Chloro-β-(2,3,4,6-tetramethylphenyl)-acrylic Acid.—Decomposition of 2.354 g. of purified less soluble salt (fraction 1) gave 0.945 g. of *l*-acid. Purification was effected by dissolving the acid in 10 cc. of ether, and 5 cc. of petroleum ether (b. p. 90–110°) and allowing the solution to stand open to the air; clusters of long white prisms, m. p. 184–185° (cor.).

Anal. Calcd. for $C_{13}H_{15}O_2Cl$: C, 65.41; H, 6.33. Found: C, 65.64; H, 6.44.

Rotation. (*l*-Acid) 0.0273 g. made up to 5 cc. with absolute ethanol at 25° gave α_D −0.195; *l*, 1; $[\alpha]^{25}D$ −35.7°.

Decomposition of purified fraction 4 in the same manner and similar recrystallization gave the *d*-acid; short, thick, white prisms, m. p. 184–185° (cor.).

Anal. Calcd. for $C_{13}H_{15}O_2Cl$: C, 65.41; H, 6.33. Found: C, 65.66; H, 6.37.

(9) Moureu, *Compt. rend.*, **137**, 260 (1902); *Bull. soc. chim.*, [3] **31**, 493, 509, 517 (1904).

(10) Arndt and Loewe, *Ber.*, **71B**, 1631 (1938).

Rotation. (*d*-Acid) 0.0292 g. made up to 5 cc. with absolute ethanol to 26° gave α_D +0.205°; *l*, 1; $[\alpha]^{26}D$ +35.7°.

Racemization of *l*-β-Chloro-β-(2,3,4,6-tetramethylphenyl)-acrylic Acid.—0.2789 g. of *l*-acid made up to 15 cc. in *n*-butanol gave α_D −0.60; after one hour, α_D −0.454; two hours, α_D −0.355; three hours, α_D −0.273; four hours, α_D −0.214; five hours, α_D −0.167; twenty-four hours α_D 0. The average half-life calculated from these values was one hundred sixty-three minutes. In a repetition of this experiment a half-life of one hundred eighty-four minutes was obtained.

Attempted Resolution of β-Methoxyl-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic Acid.—Solutions of 5.595 g. of β-methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid in 50 cc. of ethyl acetate and 6.070 g. of quinine in 100 cc. of ethyl acetate were mixed and filtered and the total volume of solvent made up to 400 cc. The cooled solution deposited 6.038 g. of salt (fraction I). Fractions of 1.355 g., 2.512 g.and 1.850 g. were removed at 250 cc., 80 cc. and by evaporation to dryness, respectively. All the fractions were obtained with the same rotation. Fraction I was separated into three fractions from ethyl acetate and the largest of these three fractions was subdivided by fractional precipitation from benzene with petroleum ether. No differentiation, as indicated by the specific rotation, could be ascertained during this fractionation. The salt obtained did not mutarotate at room temperature or at 0° and no active acid was obtained by decomposition of the salt at −5° with 10% hydrochloric acid.

Anal. Calcd. for $C_{33}H_{39}N_2O_5Br$: C, 63.56; H, 6.30; N, 4.49. Found: C, 63.20; H, 6.46; N, 4.39.

Rotation. (*l*B·*dl*A) 0.0527 g. made up to 10 cc. with absolute ethanol at 27° gave α_D −0.460; *l*, 1; $[\alpha]^{27}D$ −87.3°.

A solution of 0.500 g. of β-methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid in 5 cc. of ethyl acetate was added to a solution of 0.659 g. of *l*-brucine in 10 cc. of ethyl acetate and filtered. When the volume of the solution had reached 10 cc. by spontaneous evaporation 0.960 g. of salt was removed (fraction A). A second crop of salt weighing 0.205 g. was removed at 3 cc. These two fractions and the crops obtained by recrystallization of fraction A were obtained with the same rotation. The salt gave no evidence of mutarotation and gave no active acid when decomposed.

Rotation. (*l*B·*dl*A) 0.0293 g. made up to 5 cc. with absolute ethanol at 30° gave α_D −0.22; *l*, 1; $[\alpha]^{30}D$ −37.5°.

Summary

1. β-Bromo-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid was synthesized by addition of hydrogen bromide to 3-bromo-2,4,6-trimethylphenylpropiolic acid. It was resolved and the half-life of the active form shown to be sixty-four hours in boiling *n*-butanol. This is to be compared with a half-life of two hundred minutes for the corresponding chloro compound, β-chloro-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid, made by the action of phosphorus pentachloride on 3-bromo-2,4,6-trimethylbenzoylacetic acid.

2. β-Chloro-β-(2,3,4,6-tetramethylphenyl)-acrylic acid was resolved. The half-life was one hundred seventy-four minutes.

3. β-Methoxy-β-(3-bromo-2,4,6-trimethylphenyl)-acrylic acid was prepared from the appropriate aroylacetic acid and from the arylpropiolic acid but resolution failed.

4. The arrangement of the groups about the double bond in each of these compounds is discussed.

URBANA, ILLINOIS RECEIVED JULY 28, 1943

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Reaction of Triphenylmethylsodium with Esters of Acetylenic Acids

BY EDDIE G. LINDSTROM AND WARREN D. MCPHEE

In a previous communication from this Laboratory,[1] the 1,4-addition of triphenylmethylsodium to ethyl crotonate and methyl acrylate was reported. The study has now been extended to esters of acetylenic acids, ethyl tetrolate (ethyl 2-butynoate) and ethyl 2-pentynoate.

Ethyl tetrolate differs from ethyl crotonate only in having a triple instead of a double bond, but its reaction with triphenylmethylsodium is more complex. Less than one mole of ester is required to consume one mole of the reagent. Besides the expected ester, ethyl 3-methyl-4,4,4-triphenylcrotonate (I), there was isolated a considerable amount of the ketone, 4-methyl-1,1,1,-5,5,5-hexaphenyl-3-pentene-2-one (II).

$$(C_6H_5)_3CNa + CH_3C{\equiv}CCOOC_2H_5 \longrightarrow [(C_6H_5)_3CC(CH_3){=}CCOOC_2H_5]Na$$

$$[(C_6H_5)_3CC(CH_3){=}CCOOC_2H_5]Na + (C_6H_5)_3CNa \longrightarrow (C_6H_5)_3CC(CH_3){=}CHCOC(C_6H_5)_3$$

$(C_6H_5)_3CC(CH_3){=}CHCOOC_2H_5$ (I); $(C_6H_5)_3CC(CH_3){=}CHCOC(C_6H_5)_3$ (II)

The ketone crystallized out of the ether solution upon evaporation, and the ester remained in the filtrate. Hydrolysis of the ester afforded the crystalline 3-methyl-4,4,4-triphenylcrotonic acid.

Oxidation of 3-methyl-4,4,4-triphenylcrotonic acid with permanganate gave in low yield methyl triphenylmethyl ketone, which proved to be identical with the ketone prepared by rearrangement of the pinacol obtained from phenylbenzoin and methylmagnesium iodide. This reaction confirms the structure assigned to the acid.

Attempts to reduce 3-methyl-4,4,4-triphenylcrotonic acid to 3-methyl-4,4,4-triphenylbutyric acid[1] with Raney nickel or Adams platinum oxide catalysts at 60 pounds pressure and 75° were unsuccessful. Also, attempts to synthesize this unsaturated acid through the Reformatsky reaction of ethyl bromoacetate and methyl triphenylmethyl ketone with subsequent dehydration failed.

The formation of the ketone (II) was unexpected since the analogous reaction with ethyl crotonate gives a high yield of but one

(1) McPhee and Lindstrom, THIS JOURNAL, 65, 2177 (1943).