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

Restricted Rotation in Aryl Olefins. V. β-Bromo-β-(2-alkoxynaphthyl)-α-alkylacrylic Acids[1]

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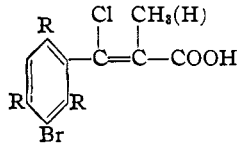
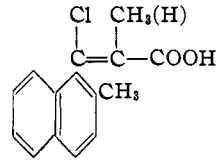
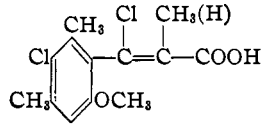
The half-life periods of the active forms of the molecules of the substituted β-arylacrylic acid type shown in I, II and III have been described in previous papers.[3]



I



II

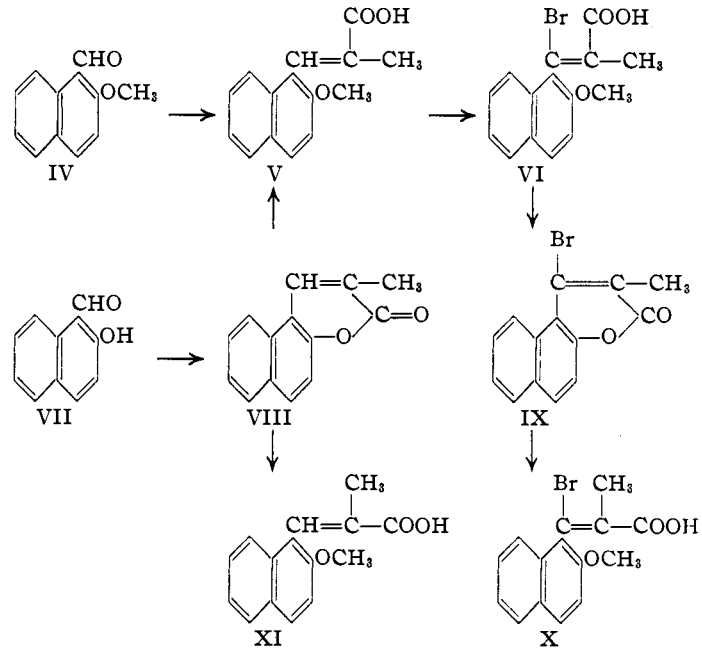


III

The remarkable stability of types I and II as contrasted to that of type III demonstrated the relatively greater steric effect of the methyl than the methoxyl when *ortho* to the acrylic acid side chain. The effect of the —CH= group of the aromatic nucleus in II is much smaller than that of an *ortho* methyl group in type I. An investigation of certain analogous derivatives from β-methoxynaphthalene was carried on simultaneously with the study of the xylenol derivatives (III). The synthesis of β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acid was accomplished and both geometric forms were obtained (VI and X). The series of reactions employed is shown in formulas IV–X.

By a Perkin synthesis with propionic anhydride and sodium propionate, β-methoxynaphthaldehyde (IV) was converted to the β-(2-methoxy-1-naphthyl)-α-methylacrylic acid (V, α-form). A single geometric isomer was always obtained. Upon bromination of compound V two atoms of bromine added to the double bond and hydrogen bromide was eliminated to give β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acid (VI, α-form). The position of the bromine in the side chain was established by oxidation of VI to β-methoxynaphthoic acid. By means of hydrobromic acid compound VI was demethylated after which rearrangement and ring closure took place with formation of 2-methyl-3-bromo-4,3-β-naphthopyrone (IX). This pyrone, on hydrolysis and methylation, gave the β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acid (X, β-form) isomeric with compound VI. From the procedure used for synthesis it is reasonable to conclude that compound X has the carboxyl *cis* to the methoxyl while in its isomer VI the carboxyl group is *trans* to the methoxyl.

β-Hydroxynaphthaldehyde (VII) by a similar Perkin synthesis led to the 2-methyl-4,3-β-naphthopyrone (VIII). Upon hydrolysis and methylation this pyrone was converted either to the acrylic acid (V) or to its geometric isomer (XI, β-form). The exact conditions for controlling the direction of this synthesis were not found. In two experiments the expected isomer (XI) resulted but in



(1) For previous paper, see Adams and Gross, THIS JOURNAL, **64**, 1786 (1942).

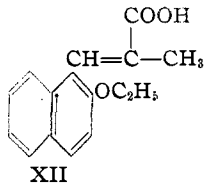
(2) An abstract of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(3) Adams and Miller, *ibid.*, **62**, 53 (1940); Adams, Anderson and Miller, *ibid.*, **63**, 1589 (1941); Adams and Binder, *ibid.*, **63**, 2773 (1941).

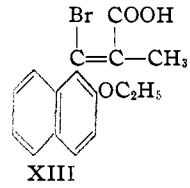
most trials rearrangement occurred and only compound V was isolated.

The assignment of the structure with the carboxyl *trans* to the methoxyl to isomer V, obtained directly from β-methoxynaphthaldehyde is based on the results (1) of similar reactions in the benzene series in which the methyl ether of salicylaldehyde gives *trans-o*-methoxycinnamic acid whereas the *cis* form is produced by hydrolysis of coumarin followed by methylation and (2) of the condensation of β-methoxynaphthaldehyde and β-hydroxynaphthaldehyde with *n*-butyric anhydride which is to be discussed later. If the formulas proposed for the brominated acids (VI and X) are correct, it must be concluded that no rearrangement occurs during bromination of compound V to form the bromo derivative (VI). The isomeric acid (XI) with the carboxyl *cis* to the methoxyl did not undergo smooth bromination. From the reaction was isolated a small amount of compound VI along with non-acidic material which was not identified. The pyrone (VIII) brominated only with difficulty and no pure substance was isolated from the product.

β-Ethoxynaphthaldehyde, in a similar Perkin synthesis, gave a single product, β-(2-ethoxy-1-naphthyl)-α-methylacrylic acid, assigned the configuration XII. It brominated to β-bromo-β-(2-ethoxy-1-naphthyl)-α-methylacrylic acid (XIII).

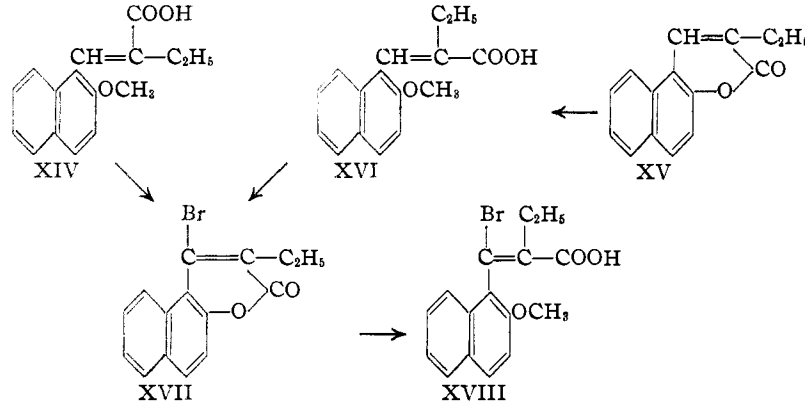


XII



XIII

β-Methoxynaphthaldehyde in a Perkin synthesis with *n*-butyric anhydride and sodium *n*-butyrate gave a single product, β-(2-methoxy-1-naphthyl)-α-ethylacrylic acid postulated as the *trans* isomer (XIV); β-hydroxynaphthaldehyde in a similar reaction yielded 2-ethyl-4,3-β-naphthopyrone (XV) which was hydrolyzed and methylated to XVI, the geometric isomer of XIV. Unlike the experience in the hydrolysis of the 2-methyl-4,3-β-naphthopyrone which yielded sometimes one and sometimes the other geometric isomer, always one product resulted which was isomeric with that from the direct condensation of the β-methoxynaphthaldehyde. Both acids (XIV and XVI) upon bromination yielded the same compound, 2-ethyl-3-bromo-4,3-β-naphthopyrone (XVII), even when the precaution was taken to have present an alkaline reagent to react with the hydrogen bromide liberated. The bromopyrone (XVII) was hydrolyzed and methylated to the β - bromo - β - (2 - methoxy - 1 - naphthyl) - α - ethylacrylic acid (XVIII).



From these experiments, it may be concluded, (1) that, in general, when no pyrone formation is possible the geometric isomer formed from the aldehyde has the carboxyl group *trans* to the alkoxyl, and (2) that the hydrolysis and methylation of a pyrone leads to an isomeric acid with the carboxyl *cis* to the alkoxyl.

Attempts to resolve acids VI, X, XIII and XVIII failed. The acids formed well-crystallized salts but only single salts which did not mutarotate were obtained and decomposition of each salt resulted in an inactive acid.

Although deductions from negative experiments on resolution are hazardous, the physical properties of these salts were so favorable that it is believed these acids cannot be resolved. If these conclusions are correct the relatively minor change in the molecule III (half-life, 173 minutes in *n*-butanol at 44°), consisting of replacement of the *ortho* methyl by a —CH= of a fused ring, serves to eliminate restricted rotation. Even the replacement of the β-methoxyl by β-ethoxyl or the α-methyl by an α-ethyl was not sufficient to render resolution possible. The bromine and chlorine atoms have been shown in the biphenyl series to have essentially the same effect, so that this modification should not alter the results.

Experimental

2-Methoxy-1-naphthaldehyde.—This was prepared either by the method of Adams and Montgomery[4] or according to the directions in "Organic Syntheses" for 2-ethoxy-1-naphthaldehyde,[5] using 2-methoxynaphthalene in place of 2-ethoxynaphthalene. Material prepared by the latter method was more easily purified.

β-(2-Methoxy-1-naphthyl)-α-methylacrylic Acid (V, α-Form).—A mixture of 9 g. of 2-methoxy-1-naphthaldehyde, 9 g. of fused sodium propionate, and 36 g. of propionic anhydride was refluxed for twenty-four hours at 170°. The mixture was poured into iced dilute aqueous sodium hydroxide, and the alkaline solution extracted with ether to remove colored impurities. Upon acidification of the aqueous solution, the product separated as a gummy mass which crystallized on rubbing. It was recrystallized from water–acetic acid mixture and then from ethanol; colorless needles, m. p. 155–156° (cor.); yield, 7.9 g. (62%).

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.35; H, 5.83. Found: C, 74.21; H, 5.87.

β-Bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic Acid. (VI, α-Form).—To 4.6 g. of β-(2-methoxy-1-naphthyl)-α-methylacrylic acid in 30 cc. of chloroform was added 3.1 g. of bromine in 15 cc. of chloroform. The solution was set aside in the dark for sixty hours. After evaporating the chloroform by means of an air stream, the solid residue was taken up in dilute aqueous potassium hydroxide, and the alkaline solution was extracted with ether to remove colored impurities. The solution was then treated with decolorizing charcoal at 90° and filtered. Upon acidification of the filtrate, the product appeared as an oil which solidified on rubbing. The material was recrystallized from water–acetic acid mixture and from ethanol giving nearly white needles, m. p. 208° (cor.); yield, 2.3 g. (38%).

Anal. Calcd. for $C_{15}H_{13}O_3Br$: C, 56.07; H, 4.08. Found: C, 55.62; H, 4.03.

The bromine was shown to be in the side chain by oxidation to 2-methoxy-1-naphthoic acid. A mixture of 0.1 g. of β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acid and 0.5 g. of potassium permanganate in 25 cc. of water was refluxed for six hours. The manganese dioxide was removed by filtration and the filtrate acidified. The fine needles which formed were filtered and recrystallized from ethanol; colorless needles, m. p. 176°. The value found in the literature for 2-methoxy-1-naphthoic acid is 176°.[5a]

2-Methyl-4,3-β-naphthopyrone (VIII).—A mixture of 5 g. of 2-hydroxy-1-naphthaldehyde,[6] 5 g. of sodium propionate, and 20 g. of propionic anhydride was refluxed at 170° for twenty-four hours. The mixture was decomposed with aqueous sodium bicarbonate solution, and the material remaining undissolved was washed thoroughly on a filter and then recrystallized from ethanol; fine white needles, m. p. 156° (cor.); yield, 4.1 g. (60%).

Anal. Calcd. for $C_{14}H_{10}O_2$: C, 79.97; H, 4.80. Found: C, 80.22; H, 4.63.

β-(2-Methoxy-1-naphthyl)-α-methylacrylic Acid. (XI, β-Form).—By heating to 90° for one hour, 4 g. of 2-methyl-4,3-β-naphthopyrone was dissolved in a solution of 2.48 g. of potassium hydroxide in 120 cc. of water. After cooling, 5.6 g. of dimethyl sulfate was added slowly with vigorous stirring. The precipitate which formed was dissolved by making the solution strongly alkaline and warming. Acidification of the resulting clear solution caused the product to separate as an oil which solidified on cooling. Several crystallizations from a water–acetic acid mixture and then four or five times from benzene resulted in the formation of thick yellow rhombs, m. p. 167° (cor.); yield, 1 g. (23%).

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.35; H, 5.83. Found: C, 74.69; H, 5.95.

Various attempts to repeat this experiment resulted sometimes in obtaining the same product and sometimes in formation of the α-form. The critical conditions for each were not found.

β-(2-Ethoxy-1-naphthyl)-α-methylacrylic Acid (XII).—From 2-ethoxy-1-naphthaldehyde,[2] by the same method used for the preparation of β-(2-methoxy-1-naphthyl)-α-methylacrylic acid, β-(2-ethoxy-1-naphthyl)-α-methylacrylic acid was obtained; white needles from water–acetic acid mixture, then from ethanol, m. p. 130° (cor.); yield 8 g. (43%).

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.97; H, 6.30. Found: C, 74.51; H, 6.32.

β-Bromo-β-(2-ethoxy-1-naphthyl)-α-methylacrylic Acid (XIII).—By bromination of 8 g. of β-(2-ethoxy-1-naphthyl)-α-methylacrylic acid in the manner described for the formation of β-bromo-(2-methoxy-1-naphthyl)-α-methylacrylic acid the bromo ethoxy derivative was obtained: white needles, m. p. 172° (cor.); yield, 3 g. (29%).

Anal. Calcd. for $C_{16}H_{15}O_3Br$: C, 57.31; H, 4.51. Found: C, 57.03; H, 4.51.

2-Methyl-3-bromo-4,3-β-naphthopyrone (IX).—A mixture of 5 g. of β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acid (VI), 15 cc. of 48% hydrobromic acid and 45 cc. of glacial acetic acid was refluxed for four hours and then poured into 400 cc. of water. The crude product which separated was filtered, taken up in chloroform and treated with decolorizing charcoal. The solvent was removed by evaporation and the residue recrystallized from ethanol; long, nearly white needles, m. p. 186° (cor.); yield, 2.5 g. (56%).

Anal. Calcd. for $C_{14}H_9O_2Br$: C, 58.13; H, 3.14. Found: C, 58.46; H, 3.42.

β-Bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic Acid (X, β-Form).—A solution of 2.5 g. of 2-methyl-3-bromo-4,3-β-naphthopyrone in 50 cc. of absolute ethanol containing 1 g. of potassium hydroxide was refluxed for ten minutes. The solvent was removed under diminished pressure on a steam cone and the residue taken up in 75 cc. of water. An additional 1 g. of potassium hydroxide was added to the solution, and then 2 g. of dimethyl sulfate, over a period of thirty minutes, with stirring. The mixture was stirred for three hours and then acidified with hydrochloric acid and extracted with ether. The ether solution was extracted with two 30-cc. portions of 5% aqueous sodium hydroxide. On acidification of the

(4) Adams and Montgomery, THIS JOURNAL, **46**, 1520 (1924).
(5) "Organic Syntheses," Vol. 20, 1940, p. 11.
(5a) Bretscher, Rule and Spence, *J. Chem. Soc.*, 1493 (1928).
(6) Adams and Levine, THIS JOURNAL, **45**, 2373 (1923).

alkaline extract the product separated as a solid which was recrystallized from ethanol: slightly yellow rhombs, m. p. 187° (cor.).

Anal. Calcd. for $C_{15}H_{13}O_3Br$: C, 56.07; H, 4.08. Found: C, 56.27; H, 4.23.

Evaporation of the ether solution resulted in the recovery of 1.5 g. of unchanged pyrone.

Bromination of β-(2-Methoxy-1-naphthyl)-α-methylacrylic Acid (XI, β-Form).—To 1 g. of β-(2-methoxy-1-naphthyl)-α-methylacrylic acid (XI) dissolved in 15 cc. of chloroform was added 0.75 g. of bromine, and the solution was set aside in the dark for twenty-four hours. The solvent was then removed by evaporation without removing the precipitate which had formed, and the residue was taken up in 150 cc. of chloroform. The chloroform solution was extracted with two 30-cc. portions of 5% aqueous sodium hydroxide. Acidification of the alkaline extract precipitated the product, which was recrystallized from glacial acetic acid. The material melted at 208° (cor.), and gave no depression of the melting point when mixed with β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acid (VI, α-form).

Evaporation of the chloroform solution yielded an alkali-insoluble material which crystallized from glacial acetic acid in fine needles; m. p. 93° (cor.); this was not investigated.

β-(2-Methoxy-1-naphthyl)-α-ethylacrylic Acid (XIV, α-Form).—The product was obtained from 20 g. of 2-methoxy-1-naphthaldehyde, 20 g. of fused potassium butyrate and 80 g. of butyric anhydride; crystallized from water–acetic acid mixture, it formed nearly colorless needles, m. p. 110° (cor.); yield, 11 g. (40%).

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.97; H, 6.30. Found: C, 75.15; H, 6.73.

Bromination of β-(2-Methoxy-1-naphthyl)-α-ethylacrylic Acid (XIV. α-Form).—Treatment of 10 g. of β-(2-methoxy-1-naphthyl)-α-ethylacrylic acid (XIV) with bromine in the usual fashion yielded no alkali-soluble material. The dark solid was extracted thoroughly with petroleum ether (b. p. 60–110°). The extract was evaporated to dryness and the solid residue crystallized repeatedly from carbon tetrachloride and finally from water–acetic acid mixture. It proved to be 2-ethyl-3-bromo-4,3-β-naphthopyrone (XVII); light brown needles, m. p. 137° (cor.); yield, 3 g. (25%).

Anal. Calcd. for $C_{15}H_{11}O_2Br$: C, 59.41; H, 3.66. Found: C, 59.98; H, 3.81.

2-Ethyl-4,3-β-naphthopyrone (XV).—From 20 g. of 2-hydroxy-1-naphthaldehyde, 20 g. of fused potassium butyrate, and 80 g. of butyric anhydride by the method used for the preparation of 2-methyl-4,3-β-naphthopyrone, 2-ethyl-4,3-β-naphthopyrone was obtained; white needles, m. p. 111° (cor.); yield, 13 g. (51%).

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.32; H, 5.40. Found: C, 80.49; H, 5.36.

β-(2-Methoxy-1-naphthyl)-α-ethylacrylic Acid (XVI, β-Form).—A solution of 10 g. of 2-ethyl-4,3-β-naphthopyrone (XV) and 6 g. of solid potassium hydroxide in 100 cc. of absolute ethanol was refluxed for ten minutes. On cooling the potassium salt separated. This was filtered and dissolved in 150 cc. of water containing 6 g. of potassium hydroxide. To this solution was added 6 g. of dimethyl sulfate over a period of thirty minutes with stirring, and the mixture was then stirred for three hours. The solution was acidified and extracted with ether and the ether solution extracted with 5% aqueous sodium hydroxide. Acidification of the alkaline extract precipitated the product. It was recrystallized from ethanol to which was added water at the boiling point of the solution until incipient turbidity; white crystals, m. p. 120° (cor.); yield, 3.5 g. (30%).

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.97; H, 6.30. Found: C, 75.13; H, 6.36.

About 3.5 g. of unchanged pyrone was recovered.

β-Bromo-β-(2-methoxy-1-naphthyl)-α-ethylacrylic Acid (XVIII).—A solution of 2 g. of 2-ethyl-3-bromo-4,3-β-naphthopyrone (XVII) in 50 cc. of absolute ethanol containing 1 g. of potassium hydroxide was refluxed for ten minutes. The solvent was then removed under reduced pressure, and the residue dissolved in 75 cc. of water to which was added 1.5 g. of solid potassium hydroxide. With stirring, 2.5 g. of dimethyl sulfate was added over a period of thirty minutes and stirring continued for three hours. The solution was then acidified, extracted with chloroform, and the chloroform solution extracted with 5% aqueous sodium hydroxide. Upon acidification of the alkaline extract the product appeared as an oil which solidified on standing. The material was recrystallized from an ethanol–water mixture; fine white needles, m. p. 138° (cor.).

Anal. Calcd. for $C_{16}H_{15}O_3Br$: C, 57.31; H, 4.51. Found: C, 57.27; H, 4.52.

From the chloroform solution 1.5 g. of unchanged pyrone was recovered.

Bromination of β-(2-Methoxy-1-naphthyl)-α-ethylacrylic acid (XVI, β-Form).—To 2 g. of β-(2-methoxy-1-naphthyl)-α-ethylacrylic acid in 16 cc. of chloroform was added 1.5 g. of bromine, and the solution was set aside in the dark for twenty-four hours. The solvent was then removed, the residue taken up in chloroform and the chloroform solution extracted with 5% aqueous sodium hydroxide. Acidification of the alkaline extract gave no product. The chloroform was evaporated and the residue recrystallized from ethanol–water mixture; light yellow needles, m. p. 137° (cor.); yield 1.5 g. (57%). This material gave no depression when melted with 2-ethyl-3-bromo-4,3-β-naphthopyrone obtained by bromination of the α-form of the acid.

Summary

1. The synthesis of the two geometric forms of β-bromo-β-(2-methoxy-1-naphthyl)-α-methylacrylic acids, one geometric form of β-bromo-β-(2-ethoxy-1-naphthyl)-α-methylacrylic acid and one geometric form of β-bromo-β-(2-methoxy-1-naphthyl)-α-ethylacrylic acid has been effected.

2. None of these molecules could be resolved. This is probably due primarily to the decreased steric effect of the —CH= group of the benzene nucleus as compared to a methyl group.

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